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ADDRESSES AND ORIGINAL ARTICLES

POSTOPERATIVE THROMBOSIS AND EMBOLISM

MORTALITY AND MORBIDITY

By Robin Pilcher, M.S.Lond., F.R.C.S.

PROFESSOR OF SURGERY IN THE UNIVERSITY OF LONDON; DIRECTOR OF THE SURGICAL UNIT, UNIVERSITY COLLEGE HOSPITAL, LONDON

Since 1929 a careful search has been made in this hospital by surgeons and registrars for cases of post-operative thrombosis and embolism. It is not claimed that no cases have been missed, but records have been kept with care since the decision was taken to make special note of these conditions. The diagnosis and recording has been made by many individuals, and the records vary in detail. The interest of all members of the staff has been a safeguard in diagnosis, doubtful cases often being submitted to consultation. For this reason, the diagnosis if recorded by a member of the staff has been accepted for purposes of this paper even when the evidence for it has not been recorded in detail.

The records for the decade 1929–38 have been analysed to show the inter-relation of thrombosis and embolism, and the mortality of the latter; the results are published in the hope that they may serve as a basis for comparison with series in which newer methods of treatment such as papaverin or heparin are used. Good accounts of these and other remedies are being published, but there is little information available as to the natural morbidity or mortality. In the series here presented prophylaxis of one sort or another has been tried, but no specific treatment of the established condition except embolectomy in one case.

CRITERIA OF DIAGNOSIS

Since it is not practicable to give case-records it is necessary to state the criteria of diagnosis and the extent to which they are fulfilled. In both thrombosis and embolism there is a rise of temperature; in a previously afebrile case this is usually noticed, and is, in fact, very often the first indication of anything amiss. In a febrile case a slight rise may be unnoticed, and when it occurs cannot be attributed necessarily to any complication. It is unusual to find no fever. In an afebrile case the onset of fever is probably the best indication of the time of onset of thrombosis. It is always a little difficult to date this accurately, and it is usual to find that the rise of temperature precedes symptoms, but sometimes it follows them. In simple thrombosis the rise is seldom of more than 1·5° F., but when embolism occurs the temperature rises higher and 101° is not uncommon. A single attack of embolism gives a characteristic rise in the temperature chart lasting about 5 days. The rise of temperature in a case of embolism often precedes the symptoms, and may be presumed to be due to undetected thrombosis.

Thrombosis has only been diagnosed in the veins of the leg. I have several times suspected hypogastric thrombosis on the symptoms described by Ducuing (1929), but have not made the diagnosis with certainty. For example, there have been two fatal cases in which unexplained retention of urine occurred a few days before death. The signs on which thrombosis is diagnosed are delayed cooling on exposure, pain and tenderness, œdema, slight cyanosis and fullness of superficial veins. Of these, the most constant are tenderness and delayed cooling; these in conjunction with a rise of temperature would be regarded as evidence of thrombosis. Sometimes the diagnosis is made first on the cooling test. A patient has an unexpected rise of temperature and the legs are exposed for ten minutes, even if they look normal. A marked difference of temperature is suggestive of thrombosis, the thrombosed leg being warmer, and I do not remember any case showing this sign alone which did not subsequently develop others. This test is vitiated by operations or inflammatory lesions on the limb in question. The degree of swelling is very variable and depends on other factors than thrombosis. The impression is widespread that cases with much œdema, the true phlegmasia alba dolens, are less subject to embolism than those with little. The signs of thrombosis enumerated above were not all present in every case. As an example, out of 141 cases of thrombosis there were 20 in which there was no rise of temperature at the time of diagnosis of thrombosis, although in some it occurred before or after. Of these 20 apparently afebrile cases of thrombosis, 9 had pulmonary embolism, some before the detection of the thrombosis. In the diagnosis of embolism little importance is attached to the presence of recognised thrombosis, and, in fact, in the majority of cases no thrombosis was found. Unless, therefore, gross errors are made in the diagnosis of embolism, it must be accepted that many cases of thrombosis are not diagnosed. The fact that thrombosis may be latent makes it difficult to assess its risks on the evidence of diagnosed cases.

Pulmonary embolism in addition to fever has three important features: pain, hæmoptysis, and signs of pleurisy or consolidation. The pain is usually pleural, and although sudden in onset does not herald the lodgment of the embolus. A large embolus produces a terrible sensation at its presumed time of impaction, but patients able to give an account of this after recovery do not describe it as pain but as a feeling of constriction of the chest associated with terror and a sense of impending death. I have several times observed hæmoptysis before pain, and this is not surprising if the pain is caused by a pleural reaction. Nor need it occasion surprise that pain is sometimes absent, since it would not be expected unless the pleural reaction were peripheral and it may be interlobar.

It is unfortunate that the case-records are often incomplete in certain particulars, but definite notes of the four features—fever, pain, hæmoptysis and signs of consolidation or pleurisy—are recorded in 68 cases out of a total of 111 non-fatal embolisms. Fever was present in all but 2: in most it was clearly associated with the embolism; in a few there was already fever and an additional rise coincided with the embolism. Pain was absent in 2 cases, hæmoptysis in 16. Physical signs of consolidation, pleurisy or both were found in all but 3 cases. All four signs were present in 48 of the 68 cases with full notes. It may appear from these figures that diagnosis has been casual, but as already stated it has only been accepted when vouched for by competent observers who have during the period taken a special interest in the disease.

ANALYSIS

The results of the analysis are given in tables I, II, and III.

TABLE I—POSTOPERATIVE THROMBOSIS AND PULMONARY EMBOLISM IN SURGICAL WARDS OF UNIVERSITY COLLEGE HOSPITAL (1929–38)

	Cases
Femoral or crural thrombosis only	98
Thrombosis with non-fatal embolism	43
Non-fatal embolism without recognised thrombosis	68
Fatal embolism	44
Thrombosis or embolism diagnosed in life followed by death from other causes	8
Total	261

TABLE II—ASSOCIATION OF THROMBOSIS AND EMBOLISM

	Cases
1. *Thrombosis diagnosed in life*—	151
With non-fatal embolism (sometimes before recognised thrombosis)	43
With fatal embolism, first attack	3
With fatal embolism, later attacks	4
With death from other causes	3
2. *Embolism diagnosed in life*—	123
With recognised thrombosis	48
Subsequent fatal attacks	10
Subsequent death from other causes	2
Fatal first attacks	34
Total embolism fatal and non-fatal	157
3. *Fatal Embolism*—	44
Thrombosis or previous attacks of embolism	13
Unexpected deaths	31

TABLE III—MORTALITY-RATES

	Per cent.
Mortality from embolism after diagnosis of thrombosis	4·6
Mortality from embolism in first attack	21·6
Mortality from embolism in survivors of first attack	8·1
Total mortality-rate of embolism	28·0
Mortality from embolism in all cases of thrombosis and embolism	16·8

As has been mentioned above, the majority of embolisms had no recognised thrombosis. It will be seen that the mortality when embolism has been diagnosed is a little higher than when thrombosis only has been diagnosed, but the difference is not statistically significant, being less than twice the standard error of the difference. In a previous paper (1937) dealing with fatal cases of embolism only I wrote that thrombosis of the veins of the leg or pelvis was found post mortem more often on the right than the left. In this, which is by contrast a clinical study, the reverse is found. The figures are given in table IV.

TABLE IV—DISTRIBUTION BY SIDES OF THROMBOSIS (A) IN NON-FATAL CASES, (B) IN FATAL CASES

	A		B	
—	Thrombosis	Embolism	Thrombosis	Embolism and percentage of embolism
Right	42	15	43	16 (37)
Left	75	20	81	25 (31)
Both	20	7	23	8
Not noted	4	1	—	—

In the cases of thrombosis diagnosed in life there is a marked preponderance of left-sided cases, although right-sided cases show a higher incidence of embolism than left. This difference is not significant, but, taken with the findings in the post-mortem study referred to, suggests that a right-sided thrombosis is more likely to be complicated by embolism than a left.

SUMMARY

(1) During the ten years 261 cases of thrombosis and embolism occurred in the surgical wards of the hospital.

(2) The mortality-rate of the whole series was 16·8 per cent. The mortality-rate of the first attack of embolism was 21·6 per cent. The total mortality-rate of embolism was 28 per cent.

(3) Fatal embolism followed 4·6 per cent. of diagnosed thromboses and 8·1 per cent. of diagnosed non-fatal embolisms. This difference is not statistically significant.

(4) In the majority of non-fatal embolisms no evidence of thrombosis was found. The majority of fatal embolisms were unexpected.

(5) Thrombosis diagnosed in life is commoner on the left side than the right. This is the reverse of the findings in a large post-mortem series of fatal embolisms.

REFERENCES

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Pilcher, R. (1937) *Brit. J. Surg.* **25**, 42.

THE ERYTHROCYTES-PLASMA INTERFACE

AND THE CONSEQUENCES OF ITS DIMINUTION

BY ROBIN FÅHRÆUS, M.D.

PROFESSOR OF PATHOLOGICAL ANATOMY IN THE UNIVERSITY OF UPPSALA

BLOOD kept in vitro at body temperature for some hours changes distinctly in certain respects. It can be either defibrinated or citrated blood but preferably blood with strong rouleaux formation and a high sedimentation-rate, such as horse's or human blood, or blood from any of those countless pathological conditions in which it has a decreased suspension stability. When such a warmed sample of blood has reached room temperature and the red corpuscles have been suspended again in the blood fluid by shaking, it becomes clear that their sedimentation-rate has been much diminished. By the exclusion of other factors or by microscopical examination it is easy to infer that the reduced sedimentation-rate of the erythrocytes depends on a reduction of their rouleaux formation. Another observation, too, can be made by microscopical comparison—namely, that the thin biconcave disks of the normal erythrocytes have grown thicker and their diameter has diminished.

The changes described (Fåhræus 1921) are as a rule well developed after warming for a few hours, and after twelve hours even the strongest rouleaux formation is usually destroyed. The sedimentation-rate of the red corpuscles is, as a result, very low perhaps only a few millimetres an hour, and they have become completely spherical. Let us say that the blood, when kept at body temperature, spontaneously increases its suspension stability.

In one respect it is easy to analyse the way in which this change comes about. It consists partly of a primary change of the corpuscles and partly of a primary change of the plasma, which in its turn has a secondary effect on the corpuscles. If red corpuscles, even when washed, are warmed separately and thereafter suspended in plasma, their rouleaux formation and sedimentation-rate are very much less than they were before warming, and the corpuscles become more spherical. If blood fluid (serum or citrated plasma) alone is warmed it changes in such a way that red corpuscles suspended in it show reduced rouleaux formation and sedimentation-rate and tend to spherocytosis—in other words, exactly the same morphological changes which the red corpuscles

undergo when they are warmed separately. The temperature range within which these changes of the blood fluid take place is 82°–118° F. (at least with horse's blood), and they are most evident at about 108·5° F.

By comparing the rise in suspension stability of whole blood with the effect produced in an artificial sample of blood in which only one chief component has been warmed, it is easy to convince oneself that the changes in the blood represent the sum of the changes in the corpuscles and in the plasma. The primary change of the erythrocytes seems to be less important in increasing the stability than the secondary, which originates in changes in the plasma. This applies in a high degree when warming takes place at normal body temperature and in a less degree at high fever temperatures. These experiments have in more recent years been continued by Bergenhem and Fåhræus (1936) and by Bergenhem (1939). During this time we have concentrated on the process in the blood fluid, from now on called the stabilisation process. The same term can be used for the process which takes place in the red corpuscles but is as yet uninvestigated.

Stabilisation Process in Blood Fluid

If red corpuscles are suspended in blood fluid which has been kept at body temperature for some hours, they become, as stated above, more or less spherical and show reduced rouleaux formation and sedimentation-rate. If this artificial blood is now centrifuged and new corpuscles are added to the clear blood fluid, the new corpuscles behave in the same way as they would in natural blood fluid—i.e., they maintain their shape, pronounced rouleaux formation, and high sedimentation-rate. This simple experiment shows that the spherocytosis and the reduced aggregation of the red corpuscles are caused by their adsorbing a substance which is formed during the warming of the blood fluid and may be called the stabilising substance.

Many circumstances point to the fact that the stabilisation process in the blood fluid is enzymatic. It has already been pointed out that it has a pronounced temperature optimum at 108·5° F. If blood fluid is heated—e.g., for ten minutes at 125° F.— it is inactivated—i.e., the formation of the stabilising substance is completely prevented, however long the blood fluid may be kept at body temperature afterwards. Further observations pointing in the same direction are that an enzyme poison, such as quinine chloride, prevents the stabilisation process, and that hydrogen-ion concentration has a great influence, the process being retarded in acid solution and strongest in a weak alkaline solution.

FORMATION OF LYSOLECITHIN

Bergenhem and Fåhræus (1936) have shown that the stabilising substance is probably identical with lysolecithin produced from serum-lecithin by a lecithinase. In any case the alcoholic extract of the stabilised blood fluid contains in much greater quantities than does the natural blood fluid a substance which contains phosphorus, which is precipitated by ether, and which when dissolved in water has a hæmolysing effect. Lysolecithin has hitherto been known as the hæmolysing substance which appears when the lecithinase of cobra venom is allowed to act on a substratum containing lecithin. This suggestion that the stabilising substance is lysolecithin is supported by the fact that the stabilisation process in serum, inactivated by heating, can be activated, and in native blood fluid intensified, by the addition of very small quantities of cobra venom. The stabilisation process therefore can be said to give blood fluid pre-hæmolytic properties. The changes which the erythrocytes undergo in stabilised plasma—i.e., spherocytosis and reduced aggregation—can be regarded as a preliminary stage to hæmolysis. The same can certainly be said also of the spherocytosis and reduced aggregation which take place when red corpuscles alone are kept at body temperature.

SEPARATION OF ERYTHROCYTES AND PLASMA

Why is the blood in vivo not changed in the same way as in vitro? Why do the red corpuscles in the vascular system keep their rouleaux formation and biconcave shape, characteristics which they lose after some hours at body temperature in vitro? Or, to put the question in another way, what is the factor which produces the stabilisation process in the in-vitro experiments?

By chance I observed that blood more or less completely kept its rouleaux formation and sedimentation-rate, and the shape of the red corpuscles unchanged when during warming it was kept flowing in the receptacle either by gentle shaking or by slow rotation. Misled by the fact that shaking of the blood fluid alone could also in certain cases hinder the stabilisation process—for reasons which were later investigated by Bergenhem (1939)—I believed at first that the inhibition by shaking was due solely to the movement of the blood. In other words, the fact that the blood was stationary, which Bergenhem and I (1936) termed the blood's "endopause," was considered to cause in some unknown way the physico-chemical conditions necessary for the stabilisation process.

Later, influenced by Knisely's (1936) studies of the spleen, we discovered that another explanation was the right one. The stabilisation process in stationary blood, both as regards blood fluid and corpuscles, is caused by the separation of these components by sedimentation of the red corpuscles. Shaking has an inhibiting influence, therefore, because it continually mixes the red corpuscles and the blood fluid. This is the only explanation for the slowing of the stabilisation process in a sample of blood which is stationary except for being shaken up some seconds every half-hour. But Bergenhem (1939) has proved that other conditions which bring the red corpuscles and the blood fluid together and thus make interaction between them possible also prevent the stabilisation process. If, for example, during the warming of stationary blood care is taken to obtain a large contact surface between the red corpuscles and the plasma by keeping a small quantity of blood in a big flat receptacle, the raising of the blood's suspension stability can be hindered nearly as effectively as by shaking.

These experiments seem to show that the red corpuscles prevent the blood fluid from receiving stabilising properties, and that the blood fluid prevents the corpuscles from being stabilised, or, in other words, blood fluid obstructs or neutralises the effect of the stabilisation process in the red corpuscles, and red corpuscles obstruct or neutralise the effect of the stabilisation process in the blood fluid. The nature of these reciprocally obstructing mechanisms is not yet known, but it can certainly be assumed that they take place upon the boundary surface between the corpuscles and the blood fluid—in other words, upon the erythrocytes-plasma interface.

The following provisional theory for the explanation of the red corpuscles' power to hinder the stabilisation process in blood fluid has been given by

Bergenhem (1939). From experiments made by Bloor (1916), Knudson (1917) and Bodansky (1931) it can be assumed that the red corpuscles play an important part in the synthesis of phosphatides and therefore in the lipoid metabolism of the blood. Because of this it is possible that the derivatives of lecithin formed by the stabilisation process in the blood fluid—i.e., lysolecithin and an unsaturated fatty acid—are adsorbed on the surface of the red corpuscles and are there resynthesised into lecithin, this then returning to the blood fluid, and so on in a continuous cycle.

No explanation, however, has been suggested of the other mechanism, which enables the blood fluid to prevent the stabilisation of the red corpuscles. Speculation cannot come into the question here before this mechanism is partly explained. The only relevant observation that I have found is that the warming of red corpuscles increases the amount of free fatty acids (Weigert 1900).

The uncertainty in these matters, however, does not extend to the question, asked above, how it comes about that blood with a low suspension stability can maintain it in the vascular system for long periods. The reason why a pneumonia patient for weeks, a pregnant woman for months, and a horse throughout its life have biconcave corpuscles with conspicuous rouleaux formation and high sedimentation-rate must be that the stabilisation process, as regards both corpuscles and blood fluid, is prevented or has its effect neutralised by the circulation of the blood, which creates the condition for interaction between its main components, an interaction which must be located at the erythrocytes-plasma interface. The question then arises whether conditions occur somewhere or at some time in the body which raise the suspension stability of the blood in the same way as this happens in stationary blood in vitro. In other words, has the organism some mechanism which brings about a temporary, but sufficiently long separation of the erythrocytes and the plasma, for the chemical changes which cause stabilisation to take place in the corpuscles, or in the blood fluid, or in both?

The Spleen as a Reservoir of Blood

As is well known, it was Barcroft (1926) who gave new life to the waning interest in the physiology of the spleen by the rediscovery and rapid advancement of our knowledge of the spleen's function as a reservoir of blood. The significance of this function seemed to be that the organism had at its disposal a reserve of blood which could be mobilised during bodily exertion. This view was confirmed by the fact that the concentration of hæmoglobin was greater in the reservoir blood of the spleen than in the circulating blood. But many have asked (Lauda 1933) whether the whole complicated anatomical structure of the spleen, which has no analogy in any other organ, has no other physiological task than to increase the quantity of circulating blood by what, in human beings at least, can only be a small percentage.

The difficult problem in the anatomy of the spleen has been its vascular system, together with the closely allied question of the blood's histological whereabouts in the spleen reservoir. Hueck's (1928) idea, the leading one not long ago, was that there could be two ways of circulation of the blood. One would be a closed circulation, with a direct connexion between the arterial capillaries and the venous sinuses, to which the circulation would be limited when the spleen was not acting as a reservoir. The open circulation, on the other hand, would be something peculiar to the spleen. By this the blood would pass from the arterial capillaries directly into the intercellular spaces of the pulp, where it would be stored while the spleen acted as a reservoir. An important point in Hueck's idea of the spleen's circulatory system was the assumption that the same anatomical units, by transforming themselves, could produce both a closed and an open circulation.

The Spleen as a Separator of Blood

Knisely's (1936) conception is very much simpler but nevertheless surprising. He experimented on living spleens of mice, rats, and cats. Microscopical examination of the blood flow shows that all the arteries open into the venous sinuses, which are linked with the smallest branches of the arteries and of the veins in the same way as ordinary capillaries. The circulation in this closed system is regulated by contractions of sphincters situated on the arterial and venous sides of the venous sinuses. The cycle for the blood's passage through the spleen can be said to begin by the closing of the sphincter on the venous side of a venous sinus. As a result of this the venous sinus begins to fill with blood and to be distended. Simultaneously a separation of the blood's main components takes place, because the blood fluid passes through the walls of the venous sinus to the intercellular spaces of the pulp. When the sinus is completely filled with red corpuscles, the sphincter on the arterial side shuts, and the corpuscles now lie freed from the blood fluid for a shorter or longer time, which in certain cases has been observed to last ten hours. Afterwards the sphincter on the venous side opens again, and the sinus empties into the veins its content of red corpuscles, which thus rejoin the circulating blood.

The ordinary histological pictures of the spleen with masses of red corpuscles in the intercellular spaces of the pulp are completely misleading, according to Knisely, and are due to the fact that in the dead or dying spleen the walls of the venous sinuses become impaired and allow the red corpuscles to pass through.

The essentials of Knisely's conception are (1) that the blood's main components are separated in the spleen because the walls of the venous sinuses form a filter, through which the blood fluid passes, while the erythrocytes do not, and (2) that the erythrocytes lie packed in the venous sinuses and separated from the blood fluid for long periods. In other words, conditions seem to be created in the spleen which ought to produce changes similar to those which take place when red corpuscles are warmed separately in vitro.

ALTERATIONS OF RED CORPUSCLES IN THE SPLEEN

Some earlier observations definitely support the suggestion that the suspension stability of the blood increases during its stay in the spleen. Thus, Hammarsten (1883) said that the red corpuscles in the spleen's blood were less flattened than those in the arterial blood, and that they had a smaller diameter—in other words, that they showed a relative spherocytosis. The correctness of this observation has been confirmed by Bergenhem and Fåhræus (1936) by comparing arterial blood and blood from the splenic vein under conditions which made certain that the latter was reservoir blood. About the same time Heilmeyer (1936) substantiated by direct measurement that the erythrocytes become more spherical during their passage through the spleen.

Further, Hammarsten (1883) said that the red corpuscles of the blood in the splenic vein showed

reduced rouleaux formation. On my advice Berglund (1930) investigated the sedimentation-rate of the blood in the spleen of horses and found on the whole a much lower rate than in arterial blood. Similar experiments were carried out later in cats by Mellgren (1939), with extra precautions which assured that actual reservoir blood was used, whereas the reaction with blood from the splenic vein was carried out with the same quantity of red corpuscles as in arterial blood. The conclusion can definitely be drawn from Mellgren's experiments that not only the sedimentation-rate but also the rouleaux formation is less in splenic blood than in arterial blood. At present it is not easy to decide whether these changes of the corpuscles in the blood of the splenic vein are direct —i.e., due to the "deplasmatised" corpuscles packed in the venous sinuses being primarily stabilised—or whether they are partly indirect—i.e., due to adsorption of the stabilising substance (lysolecithin) which is formed in cell-free plasma in the intercellular spaces of the pulp. To what extent plasma free from red corpuscles is stored in the spleen is not clear, but it seems likely that de-plasmatised erythrocytes are stored in greater quantities and longer than is the case with cell-free blood fluid. It is therefore probably also true that the stabilisation of the blood of the splenic vein is principally due to primary changes in the erythrocytes.

Hæmolysis due to Separation of Blood in the Spleen

It has long been believed that the spleen plays an important part in the physiological destruction of red corpuscles, which must be assumed to go on in the organism on a large scale. At one time it was considered that the red corpuscles were destroyed in the spleen by phagocytosis. Since Knisely (1936) has pointed out that the little we see of phagocytosis is either an agonal or a post-mortem phenomenon, this theory can be completely discarded.

The other possible method of destruction of the red corpuscles in the spleen is hæmolysis; but there is no direct evidence. For this reason Mellgren's (1939) experiments on splenic hæmolysis in cats are important. He found in the blood of the splenic vein, which came from the emptying of the splenic reservoir, a weak hæmoglobinæmia, which was soon much increased by continued hæmolysis in vitro, whereas in samples of blood from other parts of the vascular system this did not happen. The result of Mellgren's experiments can hardly be interpreted otherwise than that in the spleen hæmolytic or, more correctly, pre-hæmolytic properties are given to the blood's main components, separated in the organ, and that hæmolysis takes place when they reunite.

ENLARGEMENT OF THE SPLEEN

If the spleen's hæmolytic function is thus shown to be directly connected with its separator and reservoir function, there should be a certain parallel between hæmolysis and enlargement of the spleen—i.e., that kind of enlargement which is due not to the development of granulation tissue or tumour tissue but to an increased amount of blood. This is certainly the case to a large extent. I am thinking especially of the two physiological conditions in which erythrocytes are destroyed in increased quantities. Thus, the destruction of erythrocytes in the newborn infant produces the well-known icterus neonatorum. Åkerrén (1939) has proved that an enlarged spleen is found more often at this time than during the infant's subsequent development. The other state accompanied by an increased physiological hæmolysis is pregnancy, during which the spleen is enlarged in human beings and many animals because of hyperæmia (Seitz 1927), which certainly means nothing else but increased reservoir function.

There is also a pathological condition in which the conception that hæmolysis is a consequence of the separator and reservoir function of the spleen may be of ætiological significance—namely, hereditary hæmolytic jaundice. Naegeli (1931) and others have held that the characteristic changes in the erythrocytes—i.e., spherocytosis and reduced resistance—are the primary and essential cause of the disease. Others, however, especially Meulengracht (1918), have contended that the primary cause is the enlarged spleen. Meulengracht believes that the reduced resistance of the red corpuscles must be due to adsorbed hæmolytic substances, normally formed in the spleen, which in hæmolytic jaundice are produced there in increased quantities. Nothing has been found in the spleen in hæmolytic jaundice to contradict the assumption (Gripwall 1938) that, in this disease, it is a question of increased activity in the separation and storing of blood with consequently increased hæmolysis, as a result of the enlargement of the spleen. In this way not only the anæmia but also the spherocytosis in hæmolytic jaundice can be explained.

Reduction of Erythrocytes-plasma Interface in Circulating Blood

The alteration of the blood, which the spleen causes by separating the blood's two main components, can be explained in another way as due to the more or less complete removal of the erythrocytes-plasma interface. The relative size of this interface can also be varied in the circulating blood by two different mechanisms, of which one is easy to understand and, as Bergenhem (1939) proved, easy to demonstrate experimentally in vitro.

It is a priori clear that a certain quantity of erythrocytes in the circulating blood is necessary to hinder the stabilising process of the plasma or to neutralise its effect. Bergenhem's experiments on how artificial samples of blood with different proportions of erythrocytes behave when kept flowing at body temperature in vitro seem to indicate that blood with a normal number of red corpuscles remains unchanged, whereas blood with fewer corpuscles is stabilised. The analogy in vivo to this experimental observation in vitro is probably the fact that one finds, as a rule, a lower sedimentation-rate in secondary anæmia than would be expected from the composition of the plasma proteins and from the hydrodynamic effect exerted by an oligocytæmia of higher degree in increasing the sedimentation-rate. This was pointed out by Westergren (1924) and can now be interpreted, in my opinion, as an expression of the stabilisation of the blood in anæmia by so much adsorption of the stabilising substance formed in the blood fluid that the few corpuscles cannot neutralise it. Another fact pointing in the same direction is that the red corpuscles in secondary anæmia show a relative spherocytosis (von Boros 1937, Heilmeyer 1936).

It is of interest to remember that an important reduction of the number of erythrocytes is complicated by certain disturbances in the blood's lipoid metabolism. The so-called bleeding lipæmia in rabbits, discovered by Boggs and Morris (1909), appears as a result of repeated blood-letting, after the number of corpuscles has gone down to about 30 per cent. of the normal. A similar lipæmia can

be produced by methods that cause an intravascular hæmolysis with a like reduction in the number of corpuscles. It appears from Starup's (1937) experiments that lipæmia of this kind is quickly stopped by giving the anæmic animal transfusions of red corpuscles. If one does not assume with Starup that the oligocytæmia produces lipæmia through diminution of the blood's capacity to carry oxygen one must hold that it is due to a relative diminution of the area of the erythrocytes-plasma interface.

DECREASED SUSPENSION STABILITY OF BLOOD

I now pass over to the other mechanism, by which the erythrocytes-plasma interface can be reduced *without* a reduction of the quantity of corpuscles. It is clear that the increase in the sedimentation-rate of the red corpuscles in pregnancy and many pathological conditions has of itself no biological importance, but it may be otherwise with the phenomenon that causes the increased sedimentation-rate—i.e., the increased rouleaux formation. This is not an extravascular phenomenon. The sedimentation-rate undergoes variations in the vascular system as large as those produced in vitro. I need only call to mind that large clots of fibrin in the heart and the large vessels are only found in those pathological conditions in which the sedimentation-rate is considerably higher than normal owing to intensified rouleaux formation. The different rates of intravascular sedimentation can also be shown experimentally in healthy persons, pregnant women, and patients by puncturing a superficial vein in which the blood-stream is brought to a standstill and afterwards kept vertical for some ten minutes.

More important, however, is the fact that rouleaux certainly exist in the wholly intact blood-stream. From microscopical examination of suitable skin capillaries it has long been known that there is in certain cases a granular flow—*körnige Strömung*. German authors have wrongly explained this as due to rapid intermittent contractions in the arterioles. The granular flow is simply evidence that the red corpuscles are being transported in the blood-stream in an aggregated state. It is easy to convince oneself that there is a pronounced parallel between the degree of granular flow and the sedimentation-rate.

It is thus certain that the erythrocytes in patients with a high sedimentation-rate are aggregated into rouleaux, probably in a large part of the blood. This means that the total erythrocytes-plasma interface in all such cases is reduced.

Rouleaux formation produces an especially effective reduction of the erythrocytes-plasma interface. If we reckon that a red corpuscle is a short cylinder of diameter 8μ and height 2μ, each corpuscle has a surface of 150·8 sq. μ and ten free corpuscles have a surface of 1508 sq. μ. If, on the other hand, these ten corpuscles build a rouleau, their total free surface decreases to 603 sq. μ. It seems likely that the disk-form of the red corpuscles is biologically important in that it makes possible large variations in the size of the erythrocytes-plasma interface. It need hardly be pointed out that the erythrocytes-plasma interface, decreased through rouleaux formation, is not for any length of time formed by the same external parts of the same corpuscles. The rouleaux are continually being broken and re-formed, but this does not prevent the interface at each moment from being of a certain size, which (with equal numbers of corpuscles of the same size) depends only on the degree of the blood's suspension stability.

When the erythrocytes-plasma interface decreases in pregnancy and in infection, it can be postulated, in my opinion, that large parts of the circulating blood are exposed to somewhat the same influence as the reservoir blood of the spleen. I believe, therefore, that enlargement of the spleen and the reduction of the blood's suspension stability are related reactions, whose simultaneous appearance in pregnancy and in infections is not a mere coincidence.

The intensified rouleaux formation, which is caused by the increase of the fibrinogen and serum-globulin fractions of the plasma (Fåhræus 1921) promotes the sedimentation of the red corpuscles to such a degree that any influence exerted by the stabilisation process, as a consequence of the diminution of the erythrocytes-plasma interface, is very probably masked and difficult to elucidate.

One may ask if this second way of reducing the erythrocytes-plasma interface—i.e., rouleaux formation—is, like the above-mentioned oligocytæmia, also connected with similar disturbances of lipoid metabolism. This is clearly not the general rule, for in many infections which show a higher sedimentation-rate there is no lipæmia. However, special factors may come into play, especially fever, which, according to Ewert's (1935) experiments, considerably reduces the level of blood-cholesterol; but in fever-free conditions with reduced suspension stability it is tempting to draw the above analogy. Nephrosis is a fever-free condition with usually a very high sedimentation-rate and pronounced lipæmia. During pregnancy a lipæmia appears, which shows a pronounced parallel with the sedimentation-rate. Concerning the cause of lipæmia in pregnancy there are, as Boyd (1934) pointed out, no less than fifteen different theories. Herewith I put forward the sixteenth: that the alteration of the fat-metabolism of the blood during pregnancy is due to a decrease of the erythrocytes-plasma interface, which is very probably a significant manifestation of the decreased suspension stability of the blood.

Summary

(1) Erythrocytes and plasma, kept separate from each other, undergo—by what is called the stabilisation process—changes, which as regards the erythrocytes consist in decreased rouleaux formation and spherocytosis—alterations in direction of hæmolysis—and as regards the plasma in the formation of lysolecithin by a serum-lecithinase similar to that in cobra venom.

(2) These changes take place in the spleen—the separator of the blood—at least as regards the erythrocytes, which are kept for long periods deplasmatised in the venous sinuses of the organ (Knisely 1936), but probably also as regards the plasma, and hæmolysis takes place when separated blood components reunite in the splenic vein.

(3) The fact that the circulating blood maintains its properties depends on the fact that the stabilisation process in the erythrocytes is prevented or its effect neutralised by the plasma and vice versa—an interaction which must be located at the erythrocytes-plasma interface.

(4) The area of this interface may be diminished not only in the spleen but also in the circulating blood, with effects upon its fat-metabolism. This may occur either by the reduction of the number of erythrocytes or by increased rouleaux formation—the intravascular phenomenon which causes the increase sedimentation-rate in diseases and pregnancy.

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"INFLUENZAL" MENINGITIS

TREATED WITH M. & B. 693

REPORT OF TWO CASES

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THE treatment of "influenzal" meningitis with drugs of the sulphonamide group has been reported by Teggart (1938), Young and Moore (1938), and Taylor (1938). In two cases recovery followed. We can trace no record of "influenzal" meningitis treated with M. & B. 693, which prompts us to report the following two cases.

CASE-RECORDS

CASE 1.—A boy, aged 17 months, was admitted to the Auckland Hospital on March 2, 1939. For three weeks before admission he was somewhat fretful, but this was attributed to teething. Two days before admission there was a definite history of exposure to chill, and the next day malaise, cough, and conjunctivitis were noted.

On admission the temperature was 103° F., pulse-rate 160, and respiration-rate 74 (sleeping). The only signs present were coryza, conjunctivitis, and scattered râles throughout both lungs, suggesting acute influenza with incipient pneumonia. On the basis of this diagnosis treatment with M. & B. 693 was promptly instituted.

When seen by one of us (E. H. R.) two days after admission (fourth day of illness), the temperature was 104° F., pulse-rate 170, respiration-rate 70, and he looked seriously ill. Conjunctivitis was still present, but there were no signs of bronchitis or pneumonia. The ears were normal and the throat only slightly injected. There was no rigidity of neck or back and no Kernig. The only other features noted were undue brightness of the eyes and general irritability. There were no definite signs of meningitis, but in view of the irritability and the unexplained ill appearance of the child a lumbar puncture was done forthwith. The cerebrospinal fluid (C.S.F.) was under increased pressure and turbid. There was a definite increase of globulin. The films from the centrifuged deposit showed pus and a few gram-negative bacilli. These were mainly intracellular, as many as six bacilli being found within one polymorph cell. Cultures grew *Bacillus influenzæ*.

Treatment and progress.—On the second day of illness—i.e., on admission—M. & B. 693 was exhibited, the total for the first twenty-four hours being 2·5 g., of which probably 0·5 g. was vomited. On the third day, because of gastric intolerance, the dose was reduced to a total of 1·75 g., but vomiting still continued. On the fourth day, after the first lumbar puncture, it was realised that much larger doses would be needed, and in view of the importance of nutrition further vomiting could not be permitted. The drug was therefore suspended in sterile olive oil (1 tablet to 2·5 c.cm.) and given by intramuscular and subcutaneous injections mainly into the anterior abdominal wall. The methods of suspension in water and in normal saline, described respectively by Somers (1939) and Bryant and Fairman (1939) were not then known to us. The total dose on the fourth day was 1·5 g.

On the fifth day 3 g. of M. & B. 693 was injected, and the C.S.F. was still turbid. On the sixth day 1·75 g. was given, the C.S.F. was much clearer, and cultures were sterile. The hæmoglobin was 9·65 g. per 100 c.cm., and the leucocyte count 13,700. A small intravenous transfusion of 4 oz. of blood with 4 oz. of saline was then given. On the seventh day the hæmoglobin had risen to 12·1 g. per 100 c.cm. and the leucocyte count to 23,000. In view of this good result a further 6 oz. of blood with 7 oz. of saline was then given. The child was still very irritable, and a definite Kernig's sign and neck rigidity had developed. On the seventh and eighth days a mistake was made in the dosage of M. & B. 693, so that on each of these days only 0·13 g. was given. This error was rectified, however, and during the next five days the total dosage amounted to 9·5 g.

On the thirteenth day Dr. C. R. Burns saw the case in consultation, the point at issue being the continuance or not of administration of M. & B. 693. On the one hand, the C.S.F. had been sterile for seven days, and the injections were beginning to distress the child; on the other hand, the temperature was still 101·6° F. and pulse-rate 156, and definite signs of meningeal irritation (Kernig's sign and rigidity of the neck and back) were still present. The total dosage of the drug, allowing for losses by vomiting, had been 18 g.—i.e., just over 0·75 g. per lb. of body-weight. In view of the big dosage and its long duration (twelve days) and the probable further absorption from the oily suspension during the next few days it was decided to stop the administration of M. & B. 693 and to watch developments.

On the fifteenth day the C.S.F. was clear and colourless and contained only twelve cells per c.mm. On the twentieth day the child was sitting up, with a normal temperature, and on the twenty-seventh day he was beginning to stand. There were no physical signs, and the C.S.F. was normal except for a slight increase of pressure. On the thirty-first day he contracted an upper respiratory infection, with a spike of temperature, but this quickly subsided, and he was discharged completely well on the forty-second day. When seen two months later the child was normal in every respect.

Summary of case 1.—A boy, aged 17 months, whose illness was diagnosed on the second day as severe influenza and on the fourth as influenzal meningitis. Treatment with M. & B. 693 was begun on the second day and continued without interruption till the thirteenth day. The drug was administered orally for the first two days and subsequently by injection of an oily suspension. The total quantity given was 18 g. (0·75 g. per lb. of body-weight). Periodic examination of the hæmoglobin and leucocytes in the blood was made, and two blood-transfusions were given. Lumbar puncture for the purpose of drainage was performed daily for three days during the period of maximal dosage of the drug and subsequently for diagnostic purposes on two

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occasions. The C.S.F. was sterile on the sixth day of the illness, and thereafter the patient made a complete and uninterrupted recovery (see fig. 1).

CASE 2.—A girl, aged 12 years, first complained of frontal headache on March 19, 1939. On the following day she vomited several times and the headache became severe. On the 21st her temperature was 104° F., and she complained of stiffness at the back of her neck, and any movement induced headache. These symptoms persisted, and when she was seen on the 22nd by one of us (J. E. C.) the pulse-rate was 112, temperature 104° F., respiration-rate 20, and she was in a state of toxic delirium. She was confused and disorientated as to time and place and lay curled up in bed with knees drawn up and head somewhat extended. The ocular fundi were normal, and the pupils were 6 mm., equal, and regular, and reacted briskly to light. Ocular movements were full in all directions, and there was no diplopia, nystagmus, or strabismus. The fifth cranial nerve presented no abnormalities, and there was no weakness of the facial muscles. The remaining cranial nerves presented no abnormalities. The deep reflexes were present and equal. The tone of the lower extremities was moderately increased, the power was reduced, and coördination was unimpaired. The deep reflexes were brisk and equal, the plantar responses being flexor. There was definite rigidity of the posterior cervical muscles. The back was held rigidly, and the patient resented any attempt at flexion. Kernig's sign was obvious in both lower extremities. The ear-drums were normal, and the throat was moderately congested.

Lumbar puncture revealed a slightly turbid fluid with an opalescent appearance and under a pressure of 240 mm. The fluid contained many pus cells and gram-negative bacilli, and the globulin was increased. On culture there was an abundant growth of *B. influenzæ*. The urine contained a small amount of albumin but no pus or organisms.

Treatment and progress.—On March 22 (the fourth day of the illness) meningitis was diagnosed and treatment with M. & B. 693 begun immediately. Four tablets (2 g.) were given at 5.30 P.M. and repeated at 8.30 P.M., and thereafter two tablets were ordered two-hourly. In the first seven hours the patient received 6 g. of M. & B. 693, and at this stage there was no intolerance to the drug. During the first night she was restless, delirious, and incontinent of urine.

On the morning of the 23rd she was clearer mentally. The temperature was 102·4° F., pulse-rate 94. The administration of M. & B. 693 was continued in the same dosage (two tablets two-hourly). By 9 P.M. the temperature had fallen to 98° F., pulse-rate 84. Twenty-four tablets were given in the twenty-four hours. On the 24th at 5 A.M. the temperature was 97·8° F., and pulse-rate 72, but during the morning the patient became restless, and the temperature rose to 100° F. During this day the tablets were reduced to two four-hourly (twelve tablets in the day). Lumbar puncture showed a turbid opalescent fluid under pressure of 180 mm. and 30 c.cm. of spinal fluid was removed. A blood-count gave the following result:

Red cells ..	.. 5,470,000	Polymorphs ..	.. 62 %
White cells	.. 13,150	Lymphocytes	.. 30 %
Hæmoglobin	.. 96 %	Monocytes ..	.. 8 %
Colour-index	.. 0·89		

On March 25th her mental condition had improved, and she was taking fluids well. There was moderate cyanosis. The two tablets of M. & B. 693 were given four-hourly (twelve tablets in the day). The temperature was 101° F. at 7 P.M., and 15 c.cm. of opalescent fluid was removed by lumbar puncture. On the 26th her condition had improved, nourishing drinks were being taken well, and her diet was increased. The temperature during the day fell from 101° F. to 99·2° F. M. & B. 693 was given as before (twelve tablets in the twenty-four hours).

On March 27th the patient complained of backache and headache, and the temperature rose to 102° F. It was decided to do a further lumbar puncture to relieve the headache, and 30 c.cm. of turbid opalescent fluid was removed and the headache somewhat relieved. The fluid showed only a moderate number of pus cells and a few gram-negative bacilli, most of them lying within the polymorphs. The administration of M. & B. 693 was continued in the same dosage (twelve tablets in the twenty-four hours). A blood-count showed red cells 4,620,000, hæmoglobin 82 per cent. (12 g. per 100 c.cm.), colour-index 0·9, and leucocytes 18,900.

On the 28th the temperature fell to normal. The administration of M. & B. 693 was continued for sixteen hours (eight tablets). At this stage the patient was much improved. She was moderately cyanosed. In six days she had had 47 g. (ninety-four tablets) of M. & B. 693, had shown remarkable tolerance, and had not vomited. Our lack of facilities for the estimation of the content of the drug in the blood and C.S.F is the main justification for such massive dosage in this case. The drug was discontinued at this stage.

On March 29 lumbar puncture showed turbid fluid with an obvious increase of globulin. Films of the centrifuged deposits contained pus cells and a few gram-negative bacilli. Culture produced an abundant growth of *B. influenzæ*. It was decided at this stage to give another salt of the sulphonamide group. Proseptasine was given (two tablets four hourly for six doses). On the 30th the patient had a very comfortable day, but the temperature rose to 101° F. and the pulse-rate to 112. Proseptasine was discontinued after 6 g. had been given. On the 31st she was quieter and very drowsy. Temperature 103° F., pulse-rate 116. She was troubled with the passage of very offensive flatus.

On April 1 the temperature was 102° F., and, since the C.S.F. was still turbid and contained gram-negative bacilli and pus cells, it was decided to administer M. & B. 693 in big doses. Between 3.30 P.M. and midnight twelve tablets were given. The

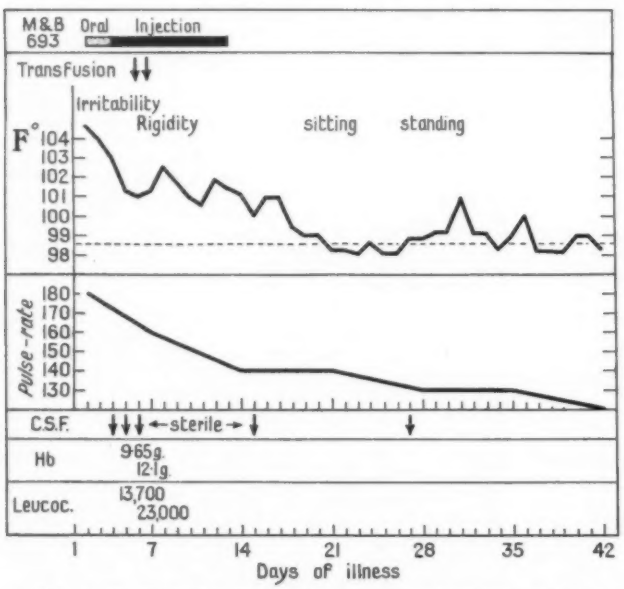

FIG. 1.—Progress of case 1. C.S.F. arrows = lumbar puncture.

patient became moderately cyanosed and restless and vomited during the night. This was the first time vomiting had occurred since the start of treatment. At this stage the case was seen by Dr. L. Ludbrook, and it was decided to give a blood-transfusion (200 c.cm.) and 5 c.cm. of the patient's father's serum intrathecally to add complement to the C.S.F.

M. & B. 693 12 g. was given on the 3rd and 6 g. on the 4th, and then administration of the drug was discontinued. Lumbar puncture showed the fluid to be under pressure of 140 mm. It was slightly turbid and contained an increased amount of globulin (334 pus cells per c.mm.), but no organisms were seen, and cultures were sterile after forty-eight hours. A blood-count gave the following result :—

Red cells	..	3,410,000
White cells	..	11,450
Hæmoglobin	..	68%
Colour-index	..	1
Polymorphs	..	70%
Lymphocytes	..	24%
Monocytes	..	4%
Eosinophils	..	2%

On the 5th the temperature rose to 102° F. A blood-transfusion of 350 c.cm. was given. Lumbar puncture on the 6th revealed a turbid fluid under pressure of 190 mm. It contained pus, increased globulin, and an occasional gram-negative bacillus. The temperature was 103° F. and the pulse-rate 110. On the 7th and 8th the temperature fell to 99° F. but rose again to 101° F. on the 9th. It was decided to administer M. & B. 693 once more. During the day twenty-four tablets were given, but the patient became moderately cyanosed, cold, and very nauseated. During the day she vomited four times. A mixture of bismuth and soda was given with the tablets, but in spite of this she continued to vomit at intervals until midnight; so administration of the drug was discontinued.

For the following four days the temperature was normal. The pulse-rate was 80–110. During this time the patient took nourishment well. On the 15th, 16th, and 17th there was a slight rise of temperature to 100° F. The blood-count on the 17th gave the following results :—

Red cells	..	4,100,000	Polymorphs	..	58%
White cells	..	8500	Lymphocytes	..	38%
Hæmoglobin	..	85%	Monocytes	..	4%
Colour-index	..	1·03			

The temperature continued to swing daily to 100–101° F., and on the 21st it was decided to give more M. & B. 693 (two tablets six-hourly) for the C.S.F. still contained an increased amount of cells, and on culture there were a few colonies of *B. influenzæ*. By the 24th the temperature had fallen to normal, although the pulse-rate remained high (100–120).

From this time the patient made an uninterrupted recovery. The pulse-rate fell to 76–80, and on May 5 there was no rigidity of the neck muscles, and there was very little stiffness of the hamstring muscles and back muscles. The patient was bright and eating well. The C.S.F. was at a pressure of 110 mm. and was colourless. There was slight increase of globulin. No organisms were seen, and cultures were sterile. The patient was discharged on the 13th and since that date has rapidly improved and is gaining weight. All rigidity of the back and legs has disappeared, and she has shown no evidence of sequelæ.

Summary of case 2.—A girl, aged 12, whose illness was diagnosed on the fourth day as influenzal meningitis, was treated with M. & B. 693 (106 g.) and proseptasine (6 g.), which were exhibited in five "bursts" of treatment. The treatment was controlled by periodic blood-counts and examinations of the C.S.F. Gastric tolerance to the drug at first was good, but subsequently vomiting occurred frequently. Blood-transfusion was used twice, and on one occasion human serum was added to the C.S.F. in an attempt to supply complement. The patient made a complete recovery. On the forty-sixth day of the illness the temperature and pulse-rate were normal, and the C.S.F. was sterile (see fig. 2).

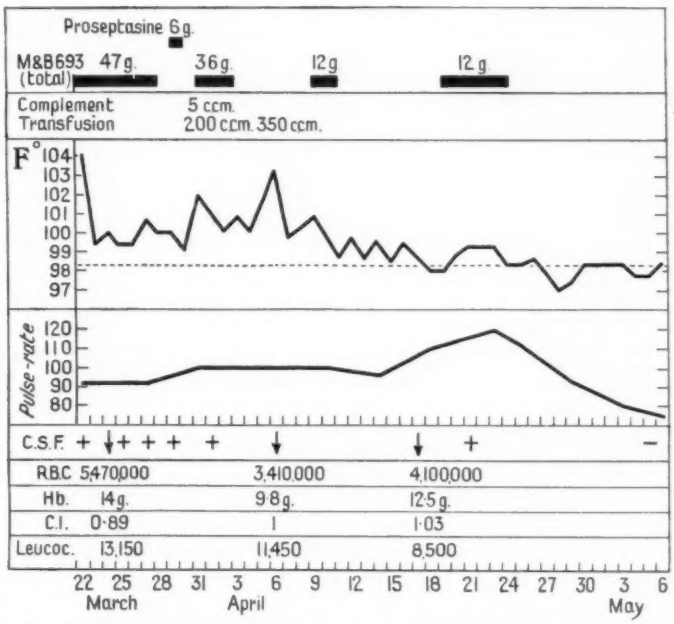

FIG. 2—Progress of case 2. C.S.F.: + = positive culture; − = negative culture; arrow = lumbar puncture.

COMMENTS

Lumbar puncture.—The therapeutic value of frequent lumbar puncture has been questioned by Banks (1938) and by McAlpine and Thomas (1939) in discussing a case of penumococcal meningitis. These workers believed that excessive drainage of the C.S.F. might be a factor in promoting the formation of adhesions round the lower brain stem with subsequent hydrocephalus; and that it lowered the concentration of the chemotherapeutic drug and so reduced its effect. If the pressure is reduced to such an extent as to allow the base of the brain to press upon the meninges surrounding the foramen magnum, the danger of subsequent adhesions seems to be very real; if, however, the pressure is maintained above the normal level we suggest that this danger is very small. The effect of the lumbar puncture on the concentration of any drug in the C.S.F. must depend on whether the drug is still being administered in full doses and on its maximal concentration maintained in the blood. We suggest that during the period of administration of M. & B. 693 any C.S.F. withdrawn will be quickly replaced by fresh fluid containing the same concentration of the drug, and in that case the removal of bacilli and toxins from the intrathecal space must do good. When, however,

the administration of the drug has been stopped, lumbar puncture should be avoided, except for purely diagnostic purposes, and then only a minimal quantity of fluid should be withdrawn.

Transfusion and complement.—In both of our cases a blood-transfusion was given twice, and we are satisfied that this played a part in the recovery of these two patients. We believe the value of transfusion to lie chiefly in the treatment of the hæmolytic anæmia induced by the sulphonamides. It might be thought that the transfusion of fresh blood would add complement to the C.S.F. However, the work of Finland et al. (1938) suggests that the C.S.F. contains no complement, so that by adding complement to the blood-stream we can only assist during the septicæmic stage of the disease. In view of Finland's findings, in case 2 we gave human serum intrathecally in an effort to add complement. McIntosh and Whitby's (1939) work suggests that the sulphonamides act by "neutralisation of some metabolic function or enzymatic activity of the organisms" and do not actively destroy them, so that by adding complement we hoped to aid the natural immunity of the body which must go hand in hand with the action of the sulphonamides. We were unable to assess the value of intrathecal complement, for its administration coincided with treatment with the drug and with the first transfusion.

M. & B. 693.—In view of the almost uniformly fatal course of influenzal meningitis in children, the recovery of two consecutive patients, one of whom was only 17 months old, cannot reasonably be ascribed to coincidence. Apart from lumbar puncture and blood-transfusion, whose inadequacy has been so conclusively proved in the past, the only treatment common to both cases was the administration of M. & B. 693. These considerations, together with the impressions gained from observation of the cases, compel us to believe that the good results obtained were pre-eminently due to this drug.

We wish to thank Dr. W. Gilmour and Dr. E. Fowler for kindly performing the pathological investigation, and Dr. L. Ludbrook and Dr. C. R. Burns, with whom we consulted frequently.

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"... The value of examinations as a test of knowledge is debatable; but it seems probable that much of the criticism levelled at the examination system should be directed, more properly, against unskilled examiners, who bring the system into disrepute by setting stupid papers and asking ambiguous questions. A well-conducted examination is a good test of knowledge and, what is even more important, constitutes a potent stimulus to effort on the part of the examinee. It is therefore desirable to hold an examination at the end of the first and of the second year of the course, though the system might be strengthened by the furnishing of reports from demonstrators in charge of the various groups of students upon the work done by each man during the year. Due consideration should be given by the examiners to these reports, which would be of special value in the examination at the end of the first year, if, as has been urged, this should be regarded as a means for elimination of the unfit."—Sir ALAN NEWTON, *Med. J. Aust.* July 15, 1939, p. 91.

VALVULAR PNEUMOTHORAX

TREATED BY MECHANICAL VALVE AND OBLITERATIVE PLEURISY

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AN analysis made by Perry (1939) of cases of spontaneous pneumothorax shows that 70 per cent. are non-tuberculous and I have the impression that my experience confirms this preponderance of non-tuberculous cases. Nevertheless, before assuming that the perforation is of non-tuberculous origin, every investigation must be made, including an inquiry into preceding malaise, loss of weight, hæmoptysis, examination of sputum and fæces for tubercle bacilli, temperature at 6.30 P.M., sedimentation-rate, and a careful scrutiny of the radiogram.

One principle of the treatment of non-tuberculous spontaneous pneumothorax, where special treatment is needed, (*a*) because of a persisting simple or valve perforation or (*b*) because of recurrent attacks, is the production of an aseptic irritation of the pleura and a small fibrinous effusion to start obliterative pleurisy. The other principle, applicable to high-pressure spontaneous pneumothorax, is a simple valve mechanism. This article describes the combination of these two principles in the management of high-pressure pneumothorax.

INDUCED OBLITERATIVE PLEURISY

The re-expansion of the collapsed lung, which can be obtained by the injection of a 5 per cent. solution of Gomenol in olive oil into the pleural cavity and by the consequent induction of obliterative pleurisy in spontaneous pneumothorax with a persistent perforation, has already been described (Chandler 1938).

Gomenol is the irritant used, because its action on the pleura is well known. It is safe if used cautiously. There is no exact dosage. Not much must be given at first, otherwise the reaction may be too severe; nor must the dose be increased too gradually, lest the pleura become accustomed to the oil and so not react. The suggested dosage is 2 c.cm. of a 2 per cent. solution, followed by 5 c.cm. of a 5 per cent. solution, 10 c.cm. of a 10 per cent. solution, and 20 c.cm. of a 20 per cent. solution. If the pleura does not then react, sodium morrhuate or else iodine might be used, but I have no experience of the use of these in the pleural cavity in spontaneous pneumothorax.

Induced obliterative pleurisy has been employed in a case of recurrent spontaneous pneumothorax.

CASE 1.—A man, aged 30, was referred to me by Dr. R. R. Fells after having had his tenth spontaneous pneumothorax. They had developed on each side at different times, being brought on by the most trivial action. When I first saw him he had a left-sided pneumothorax which was almost absorbed. I therefore advised that obliterative pleurisy should be induced on the next occasion to prevent further attacks.

Within eight weeks he had a spontaneous pneumothorax on the right side and was admitted to the London Chest Hospital. Thoracoscopy to discover the cause of the ruptures showed no bullæ of any kind on the anterior and lateral surfaces of the lung, these being the only parts visible. The lung was very pink, and there were parallel horizontal lines of pigment running regularly over the visceral pleura, as though the lung were unnaturally voluminous and, when uncollapsed, pressed unduly against the ribs

and intercostal spaces. Through the thoracoscopic cannula 5 c.cm. of a 10 per cent. solution of gomenol in olive oil was injected and 1800 c.cm. of air withdrawn.

The same afternoon the patient experienced pain at the right base and a temperature of 99° F.; and the next day some pain and tenderness, with no change of temperature. On the following day the pain had disappeared, the temperature was normal, and some fluid had appeared. The next day the fluid slightly increased, and thenceforth the lung steadily and completely re-expanded.

It is impossible to say yet whether a permanent result has been obtained nor how firm an adhesion between the two layers of the pleura is produced by this method. One can only hope that no further spontaneous pneumothorax will develop on the right side. If and when the next left-sided pneumothorax appears, the treatment will be repeated on that side.

HIGH-PRESSURE PNEUMOTHORAX WITH VALVULAR TEAR

The utmost distress to the patient and the greatest anxiety in its management may be caused by high-pressure pneumothorax with a valvular opening. It may prove fatal. Effective removal of the intrapleural air does not necessarily make the two layers of pleura adhere, and aseptic pleural irritation will not alone avail, for the rupture, acting as a one-way valve, keeps the two layers of the pleura apart. With every inspiration air comes out through the valvular tear into the pleura; with every expiration the valve closes and the air is imprisoned in the pleural cavity. With the continued repetition of these alternate events the lung is kept completely collapsed, the mediastinum is grossly displaced, and the visceral and parietal layers of pleura cannot approximate and adhere together. The two methods—the induction of obliterative pleurisy and the use of a valve mechanism—therefore must be used simultaneously. A valve can be made with a thin rubber fingerstall in the closed end of which a slit has been made. The valve in the fingerstall acts in exactly the opposite way to the valvular opening in the lung; it allows more air to escape into the atmosphere with each expiration than escapes from the lung into the pleural cavity with each inspiration, because the slit in the fingerstall can be made bigger than any probable tear in the lung, with the result that there is no high positive pressure in the pleural cavity. In a short time more air escapes through the fingerstall than escapes through the tear in the lung; so the pleural space is almost emptied of air and the pleural layers can come together, whereupon the induction of obliterative pleurisy may cause them to adhere together.

FIG. 1—Mr. Zachary Cope's self-retaining cannula.

The following case illustrates the points. It is the first time that the Cope (1939) self-retaining cannula (fig. 1) has been used for this purpose. *Canules à demeurer* were used over a century ago, especially between 1825 and 1845, for pleural effusions and empyemas, flaps of goldbeater's skin being used instead of rubber to form the valve at the opening of the cannula; so the conception of the valve mechanism is not new, but I think that the combination of methods is new.

CASE 2.—On April 20, 1939, I was asked by Dr. H. J. S. Morton to see a man, aged 58, who on getting out of bed one morning had felt a severe pain in the right chest with breathlessness. He had had to sit on the side of the bed for a time, but later he had gone down to breakfast. He had remained in the house all day but on going to bed at night had suddenly become more breathless and cyanosed.

The classical signs of spontaneous pneumothorax were found, and the patient was admitted to the London Chest Hospital, where radiography showed the heart considerably displaced to the left and practically complete collapse of the right lung (fig. 2). The patient was distressed, very cyanosed, and dyspnœic.

On the 21st 2000 c.cm. of air was withdrawn, with only transitory relief, the pressures returning to 0 + 16 cm. of water after two minutes. More air was withdrawn later, with the same result.

On the 28th a pneumothorax-refill needle was inserted into the pleural cavity in the second space anteriorly, just external to the midclavicular line. To the proximal end of the needle was tied a thin rubber fingerstall in the closed end of which a slit had been made. At the same time 2 c.cm. of a 2 per cent. solution of gomenol in olive oil was injected into the pleural cavity. There was no reaction. The valve acted excellently, and the heart returned to its normal position; but, owing to movements and cough, the end of the needle worked out of the pleural cavity into the chest wall and surgical emphysema developed.

On the 29th a long extrapleural-pneumothorax-refill needle was therefore used. This also became

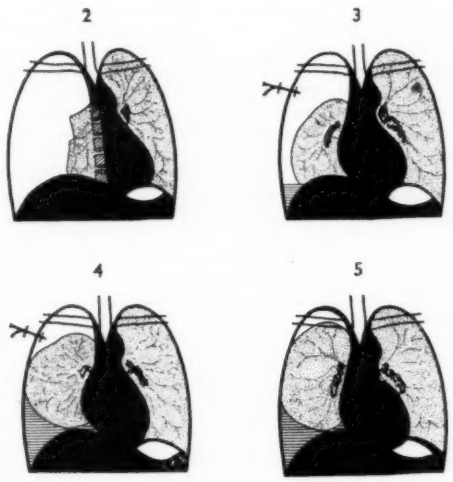

FIG. 2 (case 2)—High-pressure spontaneous pneumothorax with valvular tear, showing practically complete collapse of the right lung, displacement of the heart towards the left side and partly beyond the spine, and displacement of the trachea.

FIGS. 3 and 4 (case 2)—Re-expansion of the right lung after the insertion of the self-retaining cannula and the injection of gomenol.

FIG. 5 (case 2)—A month after the insertion of the cannula and the injection of gomenol, showing the right lung almost completely re-expanded and only a small residual pneumothorax.

displaced, causing more surgical emphysema; moreover it caused pain and became blocked.

On May 2 Cope's self-retaining cannula was used, the fingerstall being tied over the curved outer end. At the same time 10 c.cm. of a 10 per cent. solution of gomenol in olive oil was injected into the pleural cavity. The temperature did not rise, but there was some malaise and some fluid appeared.

On the 3rd the fluid increased and the patient had slight nausea. By the 13th the fluid had risen to the ninth rib posteriorly, and the lung was adhering to the diaphragm and approaching the chest wall.

From this time the lung began to re-expand steadily and became attached to the chest wall (figs. 3 and 4), and by the 12th fluid began to come through the cannula. This was therefore withdrawn on this day, with some anxiety lest the valvular opening should not have healed sufficiently firmly and the lung be stripped away from the chest wall. The patient was watched carefully, however, and nothing untoward happened. By the 18th the lung was touching the chest wall up to the third space in the midaxillary line, and the dome of the lung reached as high as the fourth rib posteriorly.

On May 21 the patient was allowed up, feeling and looking well, with the heart in the normal position. Radiography on June 1 showed the lung to be almost completely re-expanded, with a small residual pneumothorax in the uppermost part of the pleural cavity (fig. 5).

The Cope self-retaining cannula acted perfectly. It remained in position eleven days without becoming displaced. Occasionally fibrin blocked the lumen, but it was a very simple matter to remove the inner cannula, clean it, and replace it, a spigot being placed in the outer cannula meanwhile.

The most strict aseptic and antiseptic precautions were taken. The skin was kept clean with iodine and spirit and with acriflavine alternately, and the skin and the instrument were covered so far as possible with sterile dressings, leaving the fingerstall free. There was no infection of the fluid, the cannula track, or the skin. It was realised that infection was possible, but it was a risk that had to be taken. I believe that with care of every detail infection can probably be prevented.

Theoretically the self-retaining rubber catheter might be used, but there are many objections to this: collapsibility, difficulty of cleaning if blocked, and difficulty with removal and reinsertion. With the Cope self-retaining metal cannula there are no such difficulties. It might be possible to use a self-retaining rubber catheter passed through a cannula, the latter being retained permanently in position; but the catheter and cannula would have to be kept very small, and I doubt if the flange of a catheter so small would be strong enough to make it truly self-retaining. Nevertheless, in an emergency, if the Cope self-retaining cannula were not available, I believe it would be good practice to insert a stout self-retaining intercostal catheter with a fingerstall valve tied to the end. This might be the best method in traumatic pneumothorax, especially under war conditions.

SUMMARY

(1) The value of induced obliterative pleurisy in non-tuberculous spontaneous pneumothorax, previously reported in a case with a persistent perforation (Chandler 1938), is reaffirmed.

(2) A case of recurrent spontaneous pneumothorax is described in which obliterative pleurisy was induced.

(3) In high-pressure spontaneous pneumothorax with a valvular rupture of the lung it is possible to bring about the conditions suitable for the induction of obliterative pleurisy by combining this method with the use of the Zachary Cope self-retaining cannula fitted with a mechanical valve (a fingerstall with a slit). A case is described in which this was done.

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IRON ADMINISTRATION AND HÆMOGLOBIN LEVELS DURING PREGNANCY

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IT has been recognised for some time that the blood of normal non-pregnant women tends to contain less hæmoglobin than that of men (Price-Jones 1931, Widdowson and McCance 1936), and it has been suggested, in explanation of this fact, that women often have a mild but really pathological anæmia. To test this Widdowson and McCance (1936) gave iron to a group of normal men and women and observed their hæmoglobin levels. The women's hæmoglobin tended to rise and approached the men's level; the men's hæmoglobin did not change. This observation has been confirmed (Barer 1937, Sankaran and Rajagopal 1938), and from all we know of the metabolism of iron we may confidently attribute the rise to the absorption of inorganic iron. It has subsequently been found, however, that women's hæmoglobin persists at the higher levels only so long as iron continues to be administered (Barer 1937, Sankaran and Rajagopal 1938). This is a very important extension of the original observation, because iron once absorbed is not apparently re-excreted (McCance and Widdowson 1937, Widdowson and McCance 1937, McCance and Widdowson 1938). Why, therefore, should the hæmoglobin fall when the body probably contains more iron than it did while the hæmoglobin was rising? Why should it fall to a level lower than men's average level when the body contains far more iron than the average man's? Steenbock et al. (1936) noted that differentiation in the storage of iron in male and female rats appeared with sexual maturity. Castration of the female led to decreased storage. Injection of the follicular hormone into sexually immature female rats promoted greater storage than in the litter-mate controls. This is no new idea, for Bunge (1889) suggested that from puberty onwards the female stored reserves of iron for future needs of reproduction.

Children may respond to the administration of iron in the same way as adults. Mackay (1931) has recorded the prevalence of an anæmia at certain ages which can be cured with iron. It has also been noted that, if the administration of iron is stopped, the anæmia tends to recur (Josephs 1939, Mackay 1939).

The experiment here described was undertaken to obtain further evidence on this matter. It is well known that pregnant women are often anæmic, and, although probably the cause is not the same in all cases, it is generally admitted that the administration of iron will prevent the fall of hæmoglobin. It was therefore decided to study the hæmoglobin levels of pregnant

women before, during, and after periods of therapeutic medication with iron.

INVESTIGATION

Hæmoglobin determinations were made by the Haldane method on 100 women, all of whom were 20 weeks' pregnant or less, attending the antenatal department of King's College Hospital, London. The determinations were repeated a month later. Then half the women (those attending on Wednesdays) were prescribed 1000 mg. of iron, as ferric ammonium citrate or ferrum redactum, daily for six weeks. The level of hæmoglobin in the capillary blood was determined at fortnightly intervals. The administration of iron was then stopped and the hæmoglobin estimated fortnightly until a week after delivery. The other women (attending on Tuesdays) were given no medicine, and their hæmoglobin levels were observed at monthly intervals until delivery and again a week later. In both groups an estimation was always made within twenty-four hours after delivery. All determinations were made in duplicate by the same person, who did not know, while making the estimation, to whom any sample of blood belonged. At the end of the experiment it was decided not to consider (1) women whose babies were born before the thirty-sixth week; (2) women who had taken the last dose of iron within eight weeks of delivery; and (3) women in the experimental group who had not taken the prescribed iron. After these omissions 31 women were left in the "iron" group and 44 in the control group.

RESULTS

The presentation of the results is complicated by the difficulty—common to so much biological work—that, whatever the stimulus, no two individuals ever react in exactly the same way. Averaging the results is unsatisfactory in that it tends to obscure exceptional individuals who may be giving important information. The policy adopted has been to mention the exceptional cases, to give the results of a few typical individuals of both the control and the experimental groups, and to give the averaged results of both groups.

In the control series some women's hæmoglobin did not fall with the progress of pregnancy, and a very few women showed a slight rise. The characteristic response was a tendency to fall steadily throughout pregnancy and to rise sharply after delivery (figs. 1 and 3).

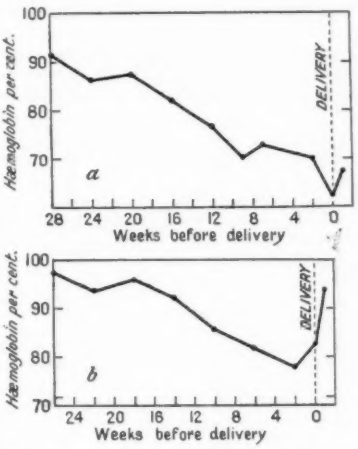

FIG. 1—Hæmoglobin curves of two pregnant women in the control group.

These results are in keeping with the work of Adair, Dieckmann, and Grant (1936), Bethell (1936) Bland, Goldstein, and First (1930), Boycott (1936), Dieckmann and Wegner (1934), Feldman et al. (1936), Fullerton (1936), Galloway (1929), Gottlieb and Gottlieb (1936), Reid and Mackintosh (1937), Strauss and Castle (1932), Toverud (1935) and require no further comment.

The cause of the fall, although possibly in some cases the result of a true deficiency of iron (Davidson et al. 1933, Mackay 1935), is probably largely due to a rise in the volume of plasma unaccompanied by a corresponding rise in the number of circulating red blood-cells (Boycott 1936, Dieckmann and Wegner 1934, Feldman et al. 1936, Strauss and Castle 1932, Thomson et al. 1938). The phenomenon is not confined to humans (Beard and Myers 1933, Van Donk et al. 1934).

The responses of the experimental group are much more complicated than those of the control because, besides the effects of pregnancy and delivery common to both groups, two further stimuli were in operation: (1) the administration of iron, and (2) the cessation of its administration. The response to iron was not an instantaneous increase in all the women's hæmoglobin concentrations. A few of the hæmoglobin curves continued to fall, as though iron had not been given at all (fig. 2*a*); several showed a break in the fall but no real rise within the six weeks of medication (fig. 2*b*); and most of them rose, some very much more than others (figs. 2*c* and *d*). The cessation of administration of iron led almost always to a fall in the hæmoglobin level of those women in whom its administration had initiated a rise. Some of the women gave as indeterminate a response to the

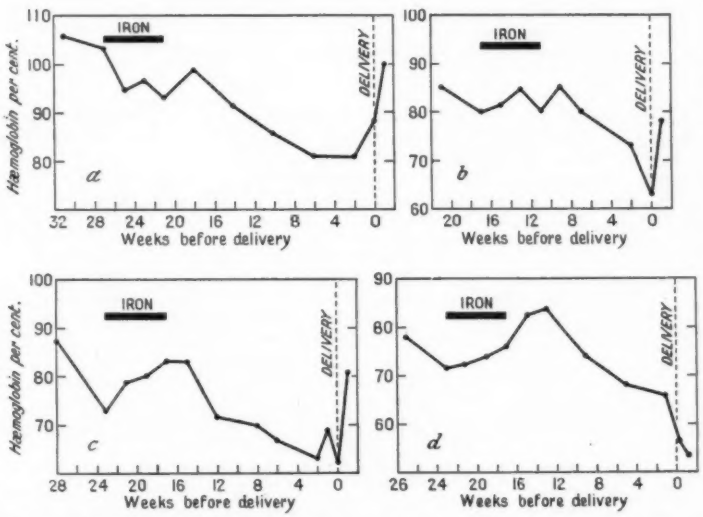

FIG. 2—Hæmoglobin curves of four pregnant women in the experimental group, showing various types of response to the administration of iron: (*a*) continued fall in spite of iron; (*b*) a break in the fall but no real rise; (*c*) and (*d*) rises.

removal of iron as they had given to its administration. The fall in hæmoglobin which manifested itself after the medication with iron had been stopped was not arrested in most cases until delivery. Fig. 3 shows the averaged results for both the control and the experimental groups. In preparing the averaged curve for the experimental group a difficulty arose in that the women started taking the iron at different stages of pregnancy. Thus it was necessary in constructing the dotted portion of the curve to average "weeks before delivery" as well as hæmoglobin values. The average time at which the first hæmoglobin estimation was made was twenty-four weeks before delivery, and the average hæmoglobin level at this stage was 93 per cent. Similarly medication with iron was started, on average, at twenty weeks before delivery and finished at fourteen weeks. The mean hæmoglobin levels at these times were 87·4 per cent. and 89·1 per cent. respectively. The important features of fig. 3 seems to be (1) the steady fall of hæmoglobin in the control group and the sharp rise after delivery; (2) the break in the fall caused by the administration of iron to the experimental group; (3) the steady fall on discontinuing its administration, so that the curve runs parallel with that of the control group; and (4) the sharp rise after delivery. The total fall in hæmoglobin level in both the experimental and the control groups is statistically significant. The difference between the levels for the two groups is not statistically significant at any one particular stage of pregnancy, but the fact that after stopping iron the curves run parallel to one another suggests that at this time the average hæmogoblin level of the experimental group really did exceed that of the controls.

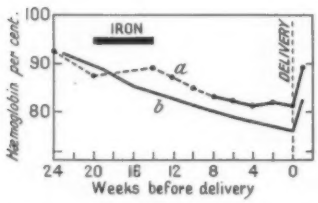

FIG. 3—Average hæmoglobin curves for (*a*) experimental and (*b*) control groups of pregnant women. For meaning of interrupted line see text.

DISCUSSION

The administration of iron has been shown by others to check the fall of hæmoglobin during pregnancy (Corrigan and Strauss 1936, Toland 1936). There is therefore nothing original in this. The fall after stopping the administration of iron is, however, a new observation and one which it is exceedingly difficult to explain. The following facts must be borne in mind: (1) the phenomenon is not peculiar to pregnancy, as was shown in the early part of this paper; (2) the administration of large (therapeutic) doses of iron for six weeks probably leads to the absorption of at least 500 mg. and possibly up to 5000 mg. of the metal, which is certainly not excreted within the period of observation—if at all (Brock and Hunter 1937, Fowler and Barer 1937, Widdowson and McCance 1937), and these amounts, moreover, are outside fœtal requirements (Coons et al. 1935, Bethell 1936); and (3) after the iron had been stopped, the experimental women's hæmoglobin level fell at the same rate as that of the controls. This requires confirmation, but it suggests that iron only stimulated the production of hæmoglobin while it was actually being administered. The body, however, was able to maintain the extra hæmoglobin in the circulation once it had been formed, but it was unable to prevent a fall in the concentration of hæmoglobin in spite of the greatly increased stores of iron. After the administration of iron had been stopped the level of hæmoglobin behaved as though iron had never been administered at all.

The following may serve as a tentative explanation of the observations. One of the many factors regulating the level of hæmoglobin in the circulation is the amount of iron in the plasma; the more there is, the more active the marrow cells become. When iron is not being administered, the amount of iron in the plasma is maintained at a low constant level by the high capacity of the storage organs. The administration of iron, however, temporarily raises the plasma iron, which stimulates the marrow to greater activity. It will be noted that this theory emphasises the amount of iron in the plasma rather than the amount in the body as the regulator of marrow activity. There is a totally different explanation, which seems improbable but is capable of direct verification—namely, that the administration of iron causes a decrease in the volume of circulating plasma.

The effects of stopping the administration of iron to women and children who have not been *proved* to be in a pathological state require rather serious consideration. The problem is as follows: does the raising of a person's hæmoglobin with massive doses of iron prove that the person was in need of iron—i.e., in a pathological state? It might very reasonably be held that, if the hæmoglobin fell to its original level when the iron was discontinued, no pathological state had been disclosed. Against this view must be set the weight of clinical opinion, which has pronounced definitely in favour of raising the hæmoglobins of babies and pregnant women. No-one has dared as yet to make any definite pronouncement about "normal" women.

If it is impossible to achieve normal hæmoglobins in babies and pregnant women by physiological means—i.e., without giving them therapeutic doses of iron—and if perfect health requires a normal hæmoglobin, clearly it is advisable to interfere with physiological processes in the best interests of the subject. This obviously raises very fundamental questions about the sanctity of the normal which it would be out of place to discuss here.

SUMMARY

(1) The administration of iron in therapeutic doses to pregnant women converted the fall in hæmoglobin, which was then in progress, into a rise.

(2) After the administration of iron had been discontinued, the hæmoglobin fell once more and at about the same rate as if iron had not been administered.

Dr. R. A. McCance has been a very great help to me in the preparation of this paper. I am indebted to the Medical Research Council for a personal grant.

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PROPHYLACTIC INOCULATION DURING THE INCUBATION PERIOD

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FROM time to time the opinion has been expressed that antityphoid inoculation undertaken during the course of a typhoid epidemic is dangerous. It has been argued that, in consequence of an alleged negative phase resulting from the inoculation, some persons acquire the disease who would otherwise have only temporarily harboured the bacteria and so escaped infection, and others develop the disease in a more virulent form who would have experienced a milder attack. No valid evidence in support of such argument is available. Indeed the only adequately controlled observations, those of Ramsey (1935), demonstrated not only that typhoid infection in inoculated contacts was not provoked, but also that, certainly after the completed set of three doses and probably after even one or two, the incidence-rate for the disease was lowered.

In view of the lack of experimental work bearing on this question and in view of remarks on this subject in the medical press (*Lancet*, 1937, *British Medical Journal* 1937, Ledingham 1937, Topley 1938) after the Croydon typhoid epidemic of 1937 it was decided to examine the effect on the death-rate of inoculations given after infection, during what may be regarded as the incubation period.

DETAILS OF EXPERIMENTS

The animal chosen was the mouse and the infecting organism *S. typhi-murium*. A mortality of 50 per cent. during an observation period of three weeks was aimed at among the controls, so that any effect the inoculations might have on the course of the disease would be indicated by either an increase or a decrease in the death-rate. In the ordinary white mouse, as purchased by the Lister Institute, an infecting dose of between one and two thousand organisms of a 24-hour broth culture of the typhi-murium strain employed, given subcutaneously between the shoulders, achieved the desired result and was given to these animals consistently throughout the experiments. The typhi-murium vaccine was administered in four daily doses, subcutaneously in alternate flanks. This system of multiple dosage was adopted with the idea of lowering the size of each individual inoculation. Since the first deaths among the infected mice take place about the seventh or eighth day, inoculation was begun forty-eight hours after infection, when the bacterium had well established itself, but there was still time to complete the vaccination before the animals began to die. As a guide to what amount of vaccine could be tolerated and be effective, in the first experiment three groups of mice were given total doses of 1·5 million, 15 million, and 150 million of a heat-killed vaccine, which, the body-weights of man and mouse being compared, represented approximately 1, 10, and 100 equivalents of the amount of T.A.B. vaccine administered prophylactically to a human being.

The vaccine, it should be noted, was killed by heating to 53° C. for 70 min. and phenolised to 0·5 per cent. after cooling. On the following day 1 c.cm. was tested for sterility and after three days, being seen to be sterile, used in the experiment. This was the only occasion on which a heat-killed vaccine so recently prepared was employed.

The results of this experiment (table I) show clearly that, whereas the smallest vaccine dose is without effect, the two larger doses definitely are damaging to the animals, almost double the number of mice dying in each of these groups. There was, however, one qualifying thought to be taken into consideration. The vaccine given had produced local reactions in over half of the animals receiving the highest dose; some showed these subcutaneous infiltrations the day following the second dose of 20×10^6 organisms and others after the third dose of 40×10^6, no examination having been made after the last inoculation. Since much larger doses of typhi-murium vaccine had often been given in other experiments to mice without such reactions being noticed, it seemed possible that this particular batch of vaccine might somehow be responsible for the reactions. An unusual feature of the batch was its recent manufacture, only four days having elapsed since it had been heated and phenolised. Its sterility had been proved by subculture of 1 c.cm. The possibility of an unusual toxicity, perhaps associated with its recent preparation, remained.

TABLE I—FRESHLY KILLED VACCINE

Vaccine administered in 4 doses		Mice	After 21 days		A.L.F.
			Dead	Percentage survivors	
$1·5 \times 10^6$	organisms heat-killed	24	10	58	14
15×10^6	organisms heat-killed	24	17	29	11
150×10^6	organisms heat-killed	24	17	29	15
Controls		24	9	62	13

A.L.F. = Average length of life in days of those dying during the period of observation.

A second experiment was therefore planned in which a more mature vaccine was used; it had been killed with chloroform at 37° C. for 15 min. six weeks previously. Two groups of mice were given 6×10^6

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and 600 × 10^6 organisms each in four doses as on the first occasion, but a further two groups were added which were given the same doses a fortnight before the infecting dose to establish contrastingly the ordinary prophylactic value of such doses. Special attention was paid to the development of subcutaneous reactions after vaccination; but, although the doses in the groups receiving the larger amount

TABLE II—VACCINE KILLED SIX WEEKS PREVIOUSLY

Vaccine administered in 4 doses	Mice	After 21 days		A.L.F.
		Dead	Percentage survivors	
6×10^6 organisms chloroform-killed before infection	24	5	79	17
600×10^6 organisms chloroform-killed before infection	24	1	96	19
6×10^6 organisms chloroform-killed in incubation period	24	5	79	15
600×10^6 organisms chloroform-killed in incubation period	24	13	43	15
Controls	24	12	50	14

varied from 40 × 10^6 on the first inoculation to 320 × 10^6 on the fourth, no sign of such inflammatory infiltrations as had been observed with the first vaccine was now noticed either in the mice inoculated prophylactically or in those receiving vaccine during the incubation period. One might infer from this that the unusual toxicity exhibited by the first heat-killed vaccine was not present in this second chloroform-killed vaccine. Table II summarises the results.

In this second experiment no detrimental effect of vaccination during the incubation period is to be noted. Even among the mice given the large amount of 600 million organisms, which represents, body-weight for body-weight, the equivalent of 400 human T.A.B. doses, no significant increase in mortality is observable, and the same dose prophylactically administered protected all but one for the period under observation, which indicates that the protective effect of the larger dose is not fully developed in the short time available when it is given during the incubation period, or that its immunising power is partly annulled by some detrimental effect. On the other hand, the smaller dose of 6 million organisms has more than halved the numbers dying among the controls. The same effect was produced by that dose given prophylactically.

In a suitable dose vaccination in the incubation period has protected and in no wise proved detrimental to the inoculated animals. It seemed increasingly likely that the poor results achieved in the first experiment were due to an unusual toxicity in the vaccine employed.

A further set of experiments was now devised to compare other vaccines killed in various fashions: (1) heat-killed and (2) chloroform-killed, as on the previous occasions; (3) heated at 60° C. for two hours without subsequent phenolisation; and (4) chloroform-killed but given fresh on the day of manufacture. An exact repetition of the first 53°-killed vaccine was not attempted, for the exact day on which those organisms which survive this heating succumb to the phenol is not predictable, and the intention was to give as freshly prepared a vaccine as possible. In all other cases the vaccines were at least a month old.

In one experiment an antityphoid vaccine was included to consider its possible non-specific effect. Another experiment tested the influence of an enteritidis vaccine on the course of an enteritidis infection. Protection was not expected in this case, because, in my experience, with no vaccine, short of a living avirulent one, can mice be adequately immunised against infection with *S. enteritidis*; but, should vaccination in the incubation period exacerbate infection, this would be observable in an acceleration of the death-rate. The infective dose in this case consisted of 6000 organisms of a 24-hour 37° broth culture injected subcutaneously between the shoulders; four daily inoculations were given subcutaneously in alternate flanks, the first being given forty-eight hours after infection. In one typhi-murium experiment the custom of vaccinating with four daily doses was varied and the same amount of vaccine administered in two inoculations on the second and third days after infection. If possible, from an immunological point of view, this method of administration would obviously be preferable. The results of these experiments are given in tables III and IV.

From table IV one learns that enteritidis vaccine given as in the previous typhi-murium experiments has no influence on the course of the infection; in each group there are but 2 or 3 survivors after twenty-one days, and the average length of life is the same. There is no evidence of any provocative action.

Table III demonstrates once again—this time with three different preparations—that typhi-murium vaccine administered during the incubation period does not exacerbate the infection but on the contrary significantly lowers the mortality of the treated mice; that inoculation of the vaccine in two, instead of four, doses is an effective mode of administration; that non-specific treatment, as afforded by an antityphoid vaccine, does not influence the course of the disease;

TABLE III—VACCINES KILLED BY DIFFERENT METHODS

Vaccine administered	Mice	After 21 days		A.L.F.
		Dead	Percentage survivors	
6 × 10^6 organisms chloroform-killed, in 4 doses	24	6	75	12
6 × 10^6 organisms 60° C. killed, in 4 doses	24	7	71	13
6 × 10^6 organisms 53° C. killed, phenolised, in 4 doses	23	7	70	14
Controls	24	13	46	13
6 × 10^6 organisms 53° C. killed, phenolised, in 2 doses	23	3	87	11
6 × 10^6 organisms chloroform-killed, fresh daily, in 4 doses	24	5	79	8
6 × 10^6 organisms, antityphoid vaccine, in 4 doses	24	7	71	13
Controls	23	7	69	13

TABLE IV—ENTERITIDIS VACCINE

Vaccine administered in 4 doses	Mice	After 21 days		A.L.F.
		Dead	Percentage survivors	
6 × 10^6 organisms, 53° C. killed, phenolised	22	19	14	11
Controls	24	22	9	11

and that freshly prepared chloroform-killed vaccine is not damaging as was the freshly prepared heat-killed vaccine of the first experiment. There were no skin reactions as with the vaccine in the first experiment, but the dosage was considerably lower than that which produced them on the first occasion.

Since treatment with two doses in place of four appeared efficient, this method was employed in the next experiment, which was undertaken to ascertain whether the rather arbitrarily chosen dose of 6 × 10^6 organisms was optimal. Batches inoculated with a

quarter of and with four times this amount were included. The results are recorded in table V.

TABLE V—EFFECTS OF VARIOUS DOSES IN A DIFFERENT STRAIN OF WHITE MICE

Vaccine administered in 2 doses	Mice	After 21 days		A.L.F.
		Dead	Percentage survivors	
1·5 × 10⁸ organisms, 53° C. killed, phenolised	24	15	37	12
6 × 10⁸ organisms, 53° C. killed, phenolised	24	13	46	11
24 × 10⁸ organisms, 53° C. killed, phenolised	24	13	46	13
Controls	24	11	54	13

In this experiment, in contradistinction to those recorded in tables II and III, vaccination of mice in the incubation period has not increased their resistance; indeed, in one group, that receiving the smallest dose, a definite increase in mortality can be observed. Since the mice employed on this occasion had been purchased from a different dealer and there was just a possibility of their possessing a diminished immunisability, animals from the original source were used with two batches of typhi-murium vaccine in an attempt to repeat the results of the earlier experiments (table VI).

TABLE VI—EFFECTS OF VARIOUS DOSES IN THE ORIGINAL STRAIN OF WHITE MICE

Vaccine administered in 2 doses	Mice	After 21 days		A.L.F.
		Dead	Percentage survivors	
6 × 10⁸ organisms, 53° C. killed, phenolised	25	7	72	14
6 × 10⁸ organisms, 53° C. killed, phenolised	23	5	78	12
Controls	26	6	77	13

The experiment recorded in table VI brings no evidence for provocation of the disease by inoculation, but there is also no evidence of immunisation. It was noticeable, too, that the strain of *S. typhi-murium* was diminishing in virulence, only 23 per cent. of the controls now dying after the usual infective dose of between one and two thousand organisms.

TABLE VII—RESULTS OBTAINED IN BLACK MICE

Vaccine administered to pure-line E mice in 2 doses	Infecting dose	Mice	Dead after 21 days	A.L.F.
6 × 10⁸ organisms, 53° C. killed, phenolised ..	1600 org.	14	14	9
Controls	1600 org.	13	13	9
6 × 10⁸ organisms, 53° C. killed, phenolised ..	193 org.	15	15	12
Controls	193 org.	15	15	12

TABLE VIII—PURE-LINE E MICE INFECTED WITH 150 ORGANISMS AND GIVEN 6 × 10⁸ ORGANISMS OF 53° C. KILLED VACCINE

Vaccine administered	Mice	Deaths occurring on days after infection														Dead	A.L.F.
		5	6	9	10	11	12	13	14	15	16	17	18	19	21		
In 2 doses	40	0	1	0	4	6	6	4	9	4	3	2	0	0	1	40	13·1
In 4 doses	39	0	0	2	1	5	8	4	5	6	2	5	0	1	0	39	14·0
Controls	40	1	0	3	3	4	5	11	4	2	6	0	1	0	0	40	12·2

To study the effect of race on animal response and to work with a mouse strain more susceptible to infection with *S. typhi-murium*, the mice used in the next experiments were Little's C.57 blacks, a pure line labelled E in this laboratory and known from previous work (Schütze et al. 1936) to be less resistant to salmonella infection. So little resistance to *S. typhi-murium* have these mice that a mortality of 100 per cent. is to be expected within three weeks, and a comparison of treated and untreated animals can rest only upon the rate at which they die. In the first of these experiments the usual infective dose of between one and two thousand organisms was given; in the later ones 193 and 150 organisms were the amounts given, so that a more prolonged incubation period might ensue. In the last experiment the effect of two doses of vaccine was compared with that of four doses; in all cases administration was begun as usual forty-eight hours after infection. The first two experiments are given in table VII, and the last in table VIII, where the daily death-rate is recorded in addition.

The results of these three experiments on pure-line mice confirm those already obtained on the ordinary white mouse. Vaccination in the incubation period has no damaging effect. The death-rate is not more rapid among the inoculated than among the controls. There is no suggestion that, whereas some favourably disposed individuals among the vaccinated have benefited from the treatment, as shown by a delayed death-rate, others less favourably disposed have fallen victims to the measure and succumbed more rapidly. Mortality among the three groups proceeds at very similar rates.

DISCUSSION OF RESULTS

An attempt to demonstrate whether prophylactic inoculation during the incubation period is harmful was carried out on mice with *S. typhi-murium* as the infecting agent and variously prepared vaccines prepared from the same strain for inoculation. By comparing the death-rate of treated and untreated animals it was hoped to estimate whether vaccination was damaging or not.

In one experiment damage resulted from the treatment, and in this case the vaccine appeared to be at fault. A four-day-old specimen had been used and was found to give unusual local reactions, an indication that the vaccine was abnormal. The cause of this abnormality was not detected; whether in spite of the satisfactory sterility test the vaccine still contained living organisms, or whether because of its recent manufacture or for some other cause it was unusually toxic, remained undecided.

In twelve other experiments, in which vaccine dosage varied from 1·5 × 10⁸ to 600 × 10⁸, only one gave a death-rate notably below that of the control; 15 treated mice died within the three weeks of experiment as compared with 11 of the controls, there being 24 in each group; the dosage on this occasion consisted of the lowest tested, 1·5 × 10⁸ organisms. Obviously such a result obtained from that number of animals is not significant. A more reliable answer will be that given where a summary of results is taken.

In the course of the various experiments on white mice 216 mice were treated with a vaccine dosage of 6 × 10⁸ organisms and had a survival-rate of 72 per cent. at the end of twenty-one days; on the other hand, only 59 per cent. of the 120 untreated controls remained alive after the same period, a clear indication that not only does vaccination in the incubation period not do harm to mice infected with *S. typhi-murium* but also that it can noticeably afford them protection. This dosage as given to the mouse

represented, body-weight for body-weight, the equivalent roughly of four times the amount of T.A.B. vaccine given to an adult human being. That the animals are not more definitely protected may well be due to the short time available for the process of immunisation. Vaccination took place on the second and third, sometimes as well on the fourth and fifth days after infection; the first death among the controls took place variously between the sixth and ninth days.

Similar tests were carried out with a pure line of mice particularly non-resistant to infection with *S. typhi-murium* and with the ordinary white mouse infected with *S. enteritidis* and treated with a corresponding vaccine. In both these cases, mortality being 100 per cent., comparison had to be made of the rate at which the animals died. The average length of life was in no way shortened by the process of inoculation. Vaccination during the incubation period was not damaging to the animals.

The conclusion, therefore, to be drawn from these experiments is that it should not be considered dangerous to inoculate a community during the course of a typhoid epidemic. If the source of infection is still undetected and possibly active, there would undoubtedly be time for prophylactic immunisation to intervene with beneficial effect. In those cases already infected with the bacterium no harm need be anticipated, and with the greater length of the incubation period in man more hope of prophylaxis may be entertained.

SUMMARY

(1) Mice were infected with *S. typhi-murium*, and two days later inoculation with a specific vaccine was begun.

(2) Such vaccination during the incubation period did not exacerbate the course of the disease.

(3) White mice (216) treated in this way showed a mortality of 28 per cent. at the end of three weeks, whereas untreated controls (120) had a mortality of 41 per cent.

(4) The average length of life of Little's C.57 black mice, a pure-line mouse particularly sensitive to infection with *S. typhi-murium*, was not decreased by vaccination in the incubation period.

(5) Vaccination with enteritidis vaccine after infection with *S. enteritidis* similarly did not accelerate the onset of the disease.

(6) The opinion is expressed that vaccination of a community during the course of a typhoid epidemic is by analogy to be recommended.

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CLINICAL NOTES

CLOSTRIDIUM WELCHII SEPTICÆMIA AND PERITONITIS IN THE PUERPERIUM

RECOVERY AFTER M. & B. 693 AND SERUM

By John K. Baker, M.R.C.S.

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Bliss and his collaborators (1939) have reported encouraging results of M. & B. 693 therapy in experimental *Clostridium welchii* infections in mice, but I have found no account of the employment of this drug in a severe human infection. Bohlman (1937) records success with sulphanilamide in surgical conditions and Sadusk and Manahan (1939) in two post-abortal septicæmias. In the following case the infection was unusually severe.

A woman aged 24, in her second pregnancy, was admitted to the Middlesex Hospital, London, on May 3 for medical induction of labour. It had been discovered by radiography that the uterus contained two fœtuses of about thirty weeks' gestation, and that the skull bones of one were overlapping; the other fœtus appeared radiologically to be anencephalic. At the end of her induction she expelled the first fœtus, which was anencephalic. At this point labour pains ceased, and it was thought advisable to await their return before attempting to deliver the second fœtus. Pitocin (3 units) was injected hourly, but after twelve hours pains had not returned. Examination then revealed the cervix about two fingers' dilated. Under anæsthesia it was dilated digitally, and the trunk and limbs of the grossly macerated second fœtus were delivered. The second head, however, remained in utero, and could only be delivered after perforation of the skull, and traction with the finger in the mouth. The placenta was expelled naturally.

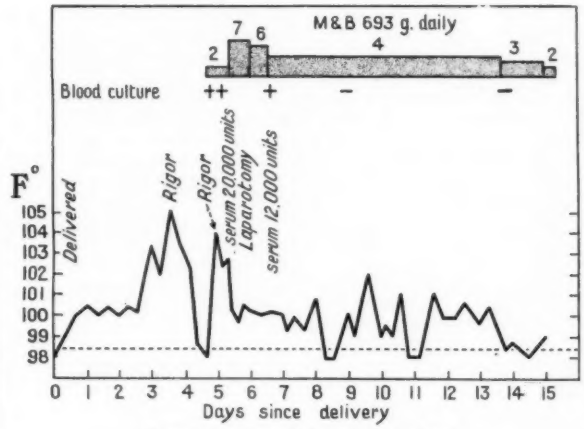
At the end of labour the temperature was 100·4° F., and twelve hours later, though the temperature was only 100° F., the lochia were noticed to be offensive, and she was transferred to Queen Charlotte's Hospital isolation block. She was then in good general condition. Forty-eight hours later she complained of lower abdominal pain, and began to pass greenish sloughs per vaginam. Later the same day she had a rigor and the temperature rose to 105° F. Glycerin was injected into the uterus and examination at this time showed induration of the parametrium on both sides. A second rigor occurred twenty-four hours after the first, and blood taken at this time yielded *Cl. welchii* on culture. Next morning—i.e., the sixth day after delivery—she developed signs of general peritonitis, with much distension. Concentrated anti-gas-gangrene serum (20,000 units) was given intravenously diluted with saline, and during the course of the day M. & B. 693 7 grammes by mouth. The abdomen was opened by Mr. L. C. Rivett in the evening under gas-and-oxygen anæsthesia, by which time her condition had become desperate.

On opening the peritoneal cavity there was an almost explosive escape of gas, and about 10 oz. of bloodstained serous effusion was found in the general cavity, the pouch of Douglas containing thick pus. Cultures from fluid taken at the time of laparotomy grew *Cl. welchii* and anaerobic streptococci, not only from the general peritoneal cavity but also from the thick pus. No attempt at hysterectomy or thorough exploration of the abdomen was made, the surgical measures being limited to drainage, through the incision, of the pouch of Douglas and the general peritoneal cavity.

At the end of the operation and for the next six hours the patient appeared to be moribund, with a bluish colour, shallow rapid respiration, and an uncountable pulse; but at the end of that time she recovered sufficiently to take more M. & B. 693 by mouth. For two days after this her condition appeared most precarious, and as she seemed profoundly toxic another 12,000 units of serum was given by the same technique on the second postoperative day. It seems probable however that the toxic appearance was due more to the M. & B. 693 than to the infection, although at this time the blood-culture was still positive for *Cl. welchii*. For a week after the opera-

tion the lochia consisted of greenish pus and sloughs of uterine muscle.

The subsequent progress may be estimated from the accompanying chart. The total of M. & B. 693 was 44 g. in nine days. Convalescence was interrupted by a severe urinary infection with *Streptococcus fæcalis*, and the formation of an inflammatory mass in the pelvis late in convalescence, both of which responded well to medical treatment. At the time of her discharge, fifty-four days after admission, the uterus was surprisingly mobile and of normal size.



Temperature and treatment chart
+ = positive blood-culture
− = negative blood-culture

Wrigley (1930) postulates certain conditions attending labour likely to be followed by gas-forming infections—viz., (*a*) the fœtus is dead for some hours in utero; (*b*) the organism must be introduced from outside the birth canal by manipulations; and (*c*) the manipulations must to some extent damage the maternal tissues in order to afford a portal of entry for the organism. All these conditions were fulfilled in the case described.

This puerperal case did not present any of the signs of hæmolysis so often noted in postabortal *Cl. welchii* septicæmias, such as hæmoglobinuria and pigmentation of skin (Hill 1936).

During the twelve hours preceding operation and in the course of the next nine days this patient received 44 g. of M. & B. 693 by mouth. It would be unwarrantable to attribute any specific action to the drug on the evidence of this case alone, especially as specific serum was administered at the same time, but the ultimate recovery from so grave an infection is very encouraging, and in view of the accumulating experimental evidence (Bliss et al. 1939, Sadusk and Manahan 1939, Buttle 1939) it seems that further trial of the drug in *Cl. welchii* infections is justified.

The total dose of serum in this case was only 32,000 units. In two non-fatal postpartum septicæmias reported by Hill (1936) and three postabortal cases reported by Buchanan (1932) the average dose was 243,600 units. Many patients have received much larger quantities and failed to survive.

I am indebted to Mr. L. C. Rivett and the honorary staff of Queen Charlotte's Hospital for permission to report this case, and to Dr. E. D. Hoare for the bacteriological reports, and to Mr. O. Lloyd and Dr. T. G. Williams of the Middlesex Hospital for the obstetric story. I should like to express my gratitude to Dr. Leonard Colebrook for his invaluable help in the preparation of this report.

References at foot of next column

FATAL AGRANULOCYTOSIS FOLLOWING TREATMENT WITH M. & B. 693

By Hamish Nicol, F.R.C.S.E.
consultant in venereal diseases at st. stephen's (l.c.c.) hospital, london; and
Bernard Freedman, M.B. Lond., M.R.C.P.
assistant medical officer at the hospital

Agranulocytosis is a well-known complication of sulphanilamide therapy, but only 5 cases have hitherto been reported following the use of M. & B. 693 (Barnett et al. 1939, Coxon and Forbes 1938, Johnston 1938, Sutherland 1939, Tzanck et al. 1939). In none of these was an autopsy described.

Our patient, aged 60, a hawker by trade, was admitted to St. Stephen's Hospital on May 1, 1939, with gonococcal urethral discharge for a week and a right-sided epididymo-orchitis. Apart from this (and pediculosis) he was healthy. The blood gonococcal complement-fixation test was positive, the blood Wassermann reaction negative and the blood Kahn "suspicious."

Two days after admission M. & B. 693 therapy was started; he was given 4 g. a day for five days, then 3 g. a day for a further sixteen days, making 68 g. in twenty-one days. He was also given potassium citrate 20 grains t.d.s., fomentations to the scrotum till the fourteenth day, and Iodex applications till the twenty-first day.

After seven days of treatment there was no urethral discharge, the epididymitis was subsiding, and the patient appeared in good general health. All treatment was stopped on the twenty-first day, the temperature, pulse- and respiration-rate having been normal throughout. But six days later—i.e., twenty-seven days after beginning treatment—the patient felt unwell. He complained only of malaise and frontal headache; he did not complain of his throat. In the morning his temperature rose to 103° F. There were no abnormal signs save a slight redness and "fleshiness" of the fauces. That evening the temperature was 105°. Hæmolytic streptococci were grown from a throat-swab taken at this stage.

Next morning the patient was very ill and drowsy. The face was flushed, the tongue was dry with a central brown coat, and there was white exudate on the right tonsil. The total white-cell count was 300 cells per c.mm., all cells seen being lymphocytes. Hæmoglobin, 72 per cent.; red cells, 4,360,000; colour-index, 0·83; punctate basophilia present. Urine: porphyrins, not detected; urobilin, present ++; ureorythrin, present +. He was given Pentnucleotide 10 c.cm. four times and Hepastab 4 c.cm. twice, on the day agranulocytosis was diagnosed. In the evening his condition was worse and the right tonsil was brown and becoming gangrenous. He died the next morning, forty-eight hours after the onset of symptoms, and eight days after the M. & B. 693 had been stopped.

Post-mortem findings.—Sloughing of fauces and pharynx. Right-sided epididymitis. Toxic softening of heart muscle. Lungs deeply congested, but otherwise normal. Toxic changes in liver and kidneys.

Histology.—Lymph-gland: post-mortem degeneration; no leucocytes seen; anthracosis. Spleen: post-mortem degeneration; no leucocytes seen. Bone-

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marrow (sternum): no leucopoiesis; mild active erythropoiesis.

There are several peculiar features in this case. Firstly, there was a clear interval of six days' good health between the cessation of treatment and the onset of symptoms of agranulocytosis. Barnett et al. (1939) described a fatal case of appendix abscess from which pneumococci were cultured, in which the white count did not fall till three days after cessation of M. & B. 693 administration, though this patient, unlike ours, had not yet been cured of the original condition. Death in Barnett's case was due to hæmorrhage from neck abscesses, and cannot be said to have been directly due to agranulocytosis. In the other 4 recorded cases agranulocytosis appeared during, not after, the administration.

Secondly, hæmolytic streptococci were grown from a throat-swab. Did these bear any causal relationship to the agranulocytosis? Clinically the appearance of the throat was that of the gangrenous pharyngitis of agranulocytosis. In the 5 previous case-reports throat-swabs are not mentioned.

Thirdly, there was gross reduction of the lymphocytes (300 per c.mm.) and complete disappearance of the granular cells. This indicates a depression of all the leucopoietic tissues, and the microscopical appearances of spleen, lymph-gland and bone-marrow correspond. The patient died before a platelet-count was performed but, as far as could be determined from the ordinary stained film, their numbers were approximately normal. The state of the leucopoietic tissues was not reported on in the 5 cases already referred to. In those of Coxon and Forbes and Barnett et al. there was gross reduction of all types of white cells, the total counts being 100 and 75 respectively. In Johnston's, Tzanck's and Sutherland's cases, however, the lymphocyte-count was within normal limits, the figures being 2200, 1000 and 1500 respectively, with polymorphs at zero.

Our patient received 68 g. of M. & B. 693 in twenty-one days. This is comparable to the dosages in the other cases—namely:

Sutherland	..	52 g. in eighteen days. Streptococcal puerperal sepsis.
Coxon and Forbes	..	54 g. in seventeen days. Typhoid.
Barnett et al.	..	80·9 g. in twenty-six days. Appendix abscess.
Johnston	..	54 g. in eleven days. Streptococcal endocarditis.
Tzanck et al.	..	18 g. in fifteen days. Lobar pneumonia.

We wish to thank Sir Frederick Menzies, medical officer of health for the county of London, and Dr. D. S. Sandiland, medical superintendent of St. Stephen's Hospital, for permission to publish the clinical details of this case; Mr. Neville Stafford, H.M. coroner for West London, and Dr. Keith Simpson for permission to publish the post-mortem report, and Dr. G. W. Goodhart, pathologist to the L.C.C. Group Laboratory, for preparing and reporting on the sections.

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MEDICAL SOCIETIES

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SECTION OF OBSTETRICS AND GYNÆCOLOGY

THIS section, under the presidency of Prof. R. W. JOHNSTONE (Edinburgh), discussed

Postpartum Hæmorrhage

Dr. ROBERT M. CORBET (Dublin) said that in Dublin the third stage of labour is treated in the most conservative manner possible. In about two-thirds of the normal cases the fundus is not touched after delivery until the signs of placental separation are present; in the remaining third the fundus is controlled manually, but no massage is allowed. After an operative delivery the fundus is usually controlled. Injection of the umbilical cord with saline is practised when the placenta is retained, and expression without anæsthesia has failed. It appears to be successful in about a third of the cases, but should not be relied upon in the presence of hæmorrhage. In 28,749 deliveries in three years there were only 147 cases (0·5 per cent.) in which manual removal of the placenta was required.

Postpartum hæmorrhage Dr. Corbet divided into three distinct types: (1) placental site hæmorrhage, due to premature separation of the placental margin; (2) true atonic hæmorrhage, where there is no bleeding till after delivery of the placenta; and (3) traumatic hæmorrhage, where the bleeding comes from lacerations in some part of the birth canal. The cause of partial separation is usually ill-advised handling of the uterus and premature attempts to express the placenta or else, after prolonged operative delivery, a combination of the effects of the anæsthetic and mechanical interference with the placenta. Morbid adhesion of the placenta is rare. The onset of bleeding due to partial separation was seldom sudden and severe. A little bleeding was noticed at the vulva; the fundus was found to be above the level of the umbilicus; the placenta was thought to be separated and attempts at expression were made. A quantity of clot was expressed but the placenta was still retained. The bleeding appeared to stop, and further time was given for separation; the whole process might be repeated, perhaps several times. One of the traps of postpartum hæmorrhage was that bleeding, without injury, might not produce any alteration in the patient's appearance or pulse until much blood had been lost. Up to a point, the loss was compensated for by vasomotor control, but when the limit of compensation had been passed, the patient's collapse might be sudden and profound.

Treatment was complicated by the retention of the placenta. Before starting active measures for its removal, the patient's general condition had to be considered carefully. If necessary, efforts should be directed to restoring her by means of intravenous or submammary saline, transfusion, warmth, morphia, raising the foot of the bed, and perhaps bandaging the limbs. No attempt should be made to remove the placenta until the patient's general condition had improved. Manual removal in collapsed patients was a very dangerous operation. It was essential to have a complete plan of action in one's mind and to be able to go from step to step, with speed and confidence. Dr. Corbett advised the following: (1) pass a catheter, (2) rub up the uterus and attempt to express the placenta by the Dublin method, (3) attempt to express it by Credé's method, (4) give an anæsthetic and repeat Credé's method, (5) remove the placenta manually, stop the anæsthetic, and give oxytocic drugs, (6) employ bimanual massage,

(7) give a hot intra-uterine douche, and (8) pack the uterus. The best material for packing was iodoform gauze, 6 in. wide, and long enough to pack the uterus with one piece. The pack should not be allowed to remain in for more than 24 hours and might often be removed after 8 hours, unless the hæmorrhage was of traumatic origin.

Oxytocic drugs given before the uterus was empty might produce irregular contraction and make the subsequent removal of the placenta more difficult. They should therefore not be used until exploration of the uterus has proved the absence of any hour-glass contraction. Pituitary extract (10 units) and ergometrine (0·5 mg.) might then be given intramuscularly. The ergometrine could be repeated if required as it was free from the undesirable side effects sometimes associated with pituitary extract. In carrying out the suggested plan of action, speed was essential, and valuable time was often wasted in arriving at a decision to remove the placenta manually and to pack the uterus.

In true atonic hæmorrhage, the bleeding started a variable time after delivery of the placenta, and there was no bleeding in the third stage itself. Although this type of hæmorrhage might occur after perfectly normal labours, it was more common after difficult deliveries with prolonged anæsthesia. In treating it, oxytocic drugs should be given at once. Many cases required nothing more than this and abdominal massage of the uterus. But if the bleeding continued, the treatment was the same as in the first type of hæmorrhage discussed.

In traumatic hæmorrhage, the bleeding might come from lacerations in any part of the genital tract, the worst being those of the cervix; these might involve the vaginal vault or even the lower uterine segment. In most cases, the diagnosis was made when bleeding continued in spite of the uterus being firmly contracted. Where the laceration could be exposed in its entirety stitching would control the hæmorrhage; if this was not possible, as when the laceration extended into the vaginal vault or the lower uterine segment, the laceration, the uterus and the vagina should be packed after removal of the placenta.

Investigations into the causes of maternal mortality showed that postpartum hæmorrhage was responsible for 7·5 per cent. of the deaths in New York, 6·3 per cent. in England and Wales, and 3·9 per cent. in Scotland. If this mortality was to be reduced the following points must be remembered. Anæmia must be treated during the antenatal period. Interference with the normal uterine action during the third stage must be avoided. The danger of attempting delivery through the partially dilated cervix must be realised. Failure of the normal mechanism of placental separation must be detected as early as possible. Adequate equipment must be prepared to deal with the hæmorrhage rapidly, particularly where the patient's history suggests the likelihood of bleeding. An ounce of forethought may save pints of blood.

Prof. JAMES HENDRY (Glasgow) divided cases of postpartum hæmorrhage into three grades according to the blood lost. In grade 1 the loss was a little greater than normal. In grade 2 compression of the uterus was necessary to control hæmorrhage. In grade 3 blood transfusion and drastic measures were needed.

First and second pregnancies and pregnancies from the seventh onwards had a greater tendency to fall into grade 1. Parity had no influence in producing grade 3. A long labour completed spontaneously did not predispose to postpartum hæmorrhage. On the other hand, where labour did not terminate normally and general anæsthesia was necessary, there was a greater predisposition. Gas-and-air analgesia did not increase the incidence, whereas morphia did. Spinal anæsthesia reduced blood loss quite definitely, compared with delivery under general anæsthesia. It was of great value to pull the uterus up out of the pelvis and massage it through the abdominal wall rather than push it downwards. Blood transfusion had reduced the mortality in postpartum hæmorrhage by 20 per cent. In the prevention of postpartum hæmorrhage it was important to conserve the patient's strength during labour with glucose and sedatives. In normal cases the uterus should not be touched during the third stage until the placenta had separated.

Dr. ENEAS MACKENZIE (Tain) said that, during 33 years of rural general practice, he had conducted 1301 deliveries. Of these, 32 had suffered from postpartum hæmorrhage. He considered the causes were exhaustion of the patient, shock, and fall of blood-pressure, resulting in failure of the uterine musculature to retract. The exhaustion and shock might be due to prolonged labour, too rapid labour, or over-distended uterus. The danger of postpartum hæmorrhage after the birth of an unusually large child could in part be avoided by inducing labour if a woman had gone past term. He had had no deaths from postpartum hæmorrhage.

Prof. FARQUHAR MURRAY (Newcastle) suggested that some of the rare and unaccountable hæmorrhages from an apparently normal empty uterus might be due to unusually large arterial trunks close to the placental site. He had never seen sepsis after a manual removal followed by an intra-uterine antiseptic douche, if this had been done while the patient was in fairly good condition. Delay, from a fear of causing sepsis or because the blood-loss was intermittent and slight, was responsible for many bad results. He was against packing the uterus; many cases at present treated by blood-transfusion would, he thought, do equally well on gum or glucose saline.

Dame LOUISE MCILROY (London) thought manual removal was very dangerous because of the high sepsis-rate afterwards. She did not think that morphine predisposed to postpartum hæmorrhage. She advised the injection of hot glycerin into the uterus as a hæmostatic. Miss BEATRICE TURNER (London) also spoke in support of hot glycerin as a useful hæmostatic.

Sir BECKWITH WHITEHOUSE (Birmingham) paid a tribute to the care with which obstetrics was conducted in Scotland. This was shown in the lower mortality figures for postpartum hæmorrhage as compared with England. He advised injection of pituitary extract during the third stage should hæmorrhage occur from a partially separated placenta. He was against manual removal in the absence of postpartum hæmorrhage or in cases in which the hæmorrhage could be controlled effectively by other means.

Prof. DUGALD BAIRD (Aberdeen) said that the use of spinal anæsthesia for forceps delivery greatly reduced the incidence of postpartum hæmorrhage. He deplored the use of intra-uterine douches and stressed the importance of treating secondary anæmia during pregnancy as a means of preventing serious postpartum hæmorrhage. The incidence of manual removal of the placenta in 1000 deliveries in the Aberdeen Maternity Hospital during 1938 was 0·6 per cent.

Prof. J. B. DAWSON (Dunedin) did not approve of the routine use of oxytocic drugs after normal delivery. He agreed with Professor Hendry that morphine

predisposed to postpartum hæmorrhage. He did not fear manual removal as much as some of the other speakers.

Sir EWEN MACLEAN (Cardiff) liked gas-and-air analgesia in midwifery and did not think it predisposed to postpartum hæmorrhage. He was in favour of midwives being allowed to give this analgesia.

Dr. H. R. FREDERICK (Port Talbot) said it was consoling to find that the general practitioner was not always to blame for the bad results which were at times attributed to him.

Professor JOHNSTONE (Edinburgh) commented on the divergence of opinions expressed. He did not think one could do harm by placing the hand gently on the fundus before the placenta was delivered.

Dr. CORBET, in reply, said he sympathised with the general practitioner in his obstetric difficulties. He agreed about the importance of treating anæmia in the antenatal clinic. He re-emphasised the need for conservatism in the third stage of labour and deprecated unnecessary massaging of the uterus before the delivery of the placenta.

SECTION OF PHARMACOLOGY, THERAPEUTICS AND ANÆSTHETICS

AT a meeting of this section Dr. J. ROSS MACKENZIE (Aberdeen) took the chair after Prof. DAVID CAMPBELL, the president, had opened the proceedings.

Anæsthesia in Dental Surgery

Dr. FREDA B. PRATT (Oxford), in a paper dealing with the significance of cyanosis in nitrous-oxide anæsthesia, pointed out that anæsthesia in dental surgery is usually performed upon normal healthy unpremedicated patients. In such subjects cyanosis denotes a reduction of oxygenation of the blood below normal. With anæsthetics other than nitrous oxide cyanosis signifies respiratory obstruction. With such a weak anæsthetic as nitrous oxide, it is necessary to utilise anoxia to reinforce the effect, and therefore in many patients, particularly if unpremedicated, cyanosis is unavoidable. Cyanosis is not of itself a sign of danger, nor its absence an assurance of safety. It does not occur until 5 g. of the hæmoglobin in the arterial blood is in the reduced form. The average patient has 15 g. of hæmoglobin per 100 c.cm. of blood, and will become cyanosed if he inhales a mixture containing approximately 10 per cent. of oxygen, since this is capable of oxygenating only two-thirds of the available hæmoglobin. A patient with less than this amount of hæmoglobin would not become cyanosed on the same mixture, but a patient with more would become more markedly cyanosed. Patients can be divided into plethoric, normal and anæmic types, and slides were shown to illustrate the fact that when inhaling a mixture of nitrous oxide with say 10 per cent. oxygen the plethoric patient becomes cyanosed earliest, and that a patient with severe anæmia can never become cyanosed, although he is much more depressed than the plethoric or normal patient. The danger of relying on cyanosis as a guide to the depth of anæsthesia is therefore evident. The inevitability of marked cyanosis in the plethoric patient with nitrous oxide alone was discussed. The fact that the automaticity of respiration is the cardinal sign of anæsthesia with nitrous oxide was stressed. Various methods of subduing the anæsthetic-resistant patient were reviewed.

Dr. JOHN GILLIES (Edinburgh) described the use of cyclopropane in dental surgery. He had found that the greater potency of this agent over nitrous oxide made it possible to deal easily with the unpremedicated, robust adult. After a face-mask induction of anæsthesia, the patient usually remains unconscious long enough to enable completion of the type of dental work undertaken on the ambulant subject. If necessary, anæsthesia is prolonged by nitrous oxide, administered nasally. Recovery is rapid and uneventful. In the unpremedicated patient, the secretions are stimulated by cyclopropane but not to an inconvenient degree, and the incidence of vomiting is higher than after nitrous oxide alone. All the cases undertaken had proved very successful.

Dr. W. S. MCCONNELL (London) spoke on the use of Evipan in dental surgery on ambulant patients. The evipan is injected when the patient is upright in the dental chair. The semi-reclining position is not favoured because saliva gravitates backwards, and irritates the pharyngeal wall initiating a cough. The patient is prevented from slipping by supporting him round the pelvis with a strap. A prop should be inserted before anæsthesia is begun, and the dentist should hold up the lower jaw to prevent the prop slipping in case the patient yawns. The whole of the estimated dose is injected rapidly. The nosepiece is then placed in position, and anæsthesia continued with nitrous oxide. The dose of evipan administered varies from 0·25–1·0 g. The method is especially useful for the vigorous adult and for patients who dislike induction by inhalation methods. The patient can leave the dental surgery from ½ to 1½ hr. after the operation. Chronic alcoholic patients eliminate the evipan rapidly. Pentothal is not favoured because of the marked respiratory depression following its use.

Dr. A. H. MACKLIN (Dundee) said that he had long held and taught that cyanosis is not of itself harmful but is an inevitable part of nitrous-oxide anæsthesia in the average patient. He stressed the fact that the anæmic patient can be seriously depressed from nitrous oxide, though failing to show cyanosis. In his opinion the basis of all forms of anæsthesia is asphyxia, which in the case of nitrous oxide is due to the exclusion of oxygen from the inhaled gases, and with other anæsthetics, due to the poisoning of the cells by anæsthetic which prevents their using the circulating oxygen. Regarding the general technique of dental anæsthesia, he insisted on the necessity for a tight gauze pack in the pharynx and therefore considered the administration of nitrous oxide by a nasal inhaler to be contra-indicated. He advocated the use of a pharyngeal tube.

Dr. B. E. COOK (Doncaster) stated that she used ethylene as a routine for dental work. The resulting anæsthesia, deeper than is possible with nitrous oxide, proved useful in the robust adult. It was particularly useful for children. Recovery was uneventful. She employed ethylene without any mishap in rooms where a naked flame was present.

Dr. R. J. CLAUSEN (London) stated he had found the operating conditions afforded by ethylene to be excellent for dental surgery, but after being anæsthetised by ethylene experimentally, he was impressed by the prolonged postanæsthetic depression, a factor which lowered his opinion of the usefulness of this agent in the ambulant patient.

Dr. H. W. FEATHERSTONE (Birmingham) described his personal experience of prolonged postanæsthetic depression following cyclopropane.

Dr. A. BARNSLEY (Guildford) described a simple method for facilitating venepuncture.

Dr. R. E. MANSFIELD (London) asked if Dr. Pratt considered secondary saturation a justifiable procedure

in dental work in cases where an adjuvant to nitrous oxide alone would ordinarily be necessary. She mentioned the suitability of vinesthene for dental work in children.

Dr. J. H. T. CHALLIS (London) spoke of the difficulties of dental anæsthesia in children, and of the lack of any really ideal method.

Dr. PRATT, in reply, said she considered the use of ethylene in the presence of a naked flame to be very dangerous. In her opinion there were degrees of "secondary saturation." Full saturation was dangerous for patients with failing circulation and in any case was not justified for dental extractions. There were resistant patients who could be subdued by a modified saturation—i.e., by anæsthetising them deeply with nitrous oxide for a short time and then lightening anæsthesia before extractions were commenced. For the very resistant patient she preferred to supplement light nitrous-oxide anæsthesia with evipan or ethyl chloride.

Anæsthesia in Genito-urinary Surgery

Dr. T. A. B. HARRIS (London) said that in genito-urinary work anæsthesia may be required to allow either diagnostic investigation or surgical operation. Cystoscopy in women can always be performed without an anæsthetic. In men, local, general or spinal anæsthesia can be employed. The disadvantage of general anæsthesia is its effect of diminishing urinary secretion, but evipan or Avertin followed by nitrous oxide delays the secretion of indigo-carmine for 1–2 minutes only. At St. Peter's Hospital for Stone, low-spinal anæsthesia is favoured for this procedure. If it is known that the cystoscopy will take only a short time, a satisfactory anæsthetic is Omnopon and scopolamine, followed by evipan. Pentothal is believed to produce powerful contractions of the bladder, and is therefore contra-indicated. For cases where anæsthesia is required for surgical intervention, if the patient's general condition is very poor local anæsthesia should be employed. An analysis of 24 deaths in poor-risk cases whose average age was 69, and who were dyspnœic at rest, revealed that the most important single factor increasing any risk is cardiac decompensation. In this connexion, a too-high spinal anæsthetic is dangerous because the stagnation of the circulation in the area anæsthetised provides an increase in the peripheral resistance and therefore increased strain on the heart. For this reason in renal surgery unilateral spinal anæsthesia is preferred to bilateral. Either avertin or evipan basal anæsthesia followed by general anæsthesia are satisfactory. The avertin should be washed out of the rectum just before general anæsthesia is begun, in order that it should not delay the postoperative recovery. During convalescence, massage and re-educational breathing exercises are important in preventing postoperative complications.

Dr. CLAUSEN stated that he uses opoidene-scopolamine as premedication for cases proceeding to general anæsthesia. He dislikes heavy basal anæsthesia, and does not use avertin. Divinyl ether has many advantages for general anæsthesia. Ethylene-oxygen is very satisfactory for prostatectomy.

Dr. MCCONNELL considered the all-important factor in this type of surgery to be the avoidance of anoxæmia. Evipan followed by gas, oxygen and vinesthene delivered from a drip-bottle is very satisfactory for prostatectomy. If required ether can be given in addition to the vinesthene.

Dr. P. M. OVERTON (Bolton) stated that he had found epidural anæsthesia extremely satisfactory both for genito-urinary and general abdominal surgery.

Dr. H. H. PINKERTON (Glasgow) favoured the use of cyclopropane in the poor-risk patient on account of its freedom from toxicity.

Dr. FEATHERSTONE was of opinion that a healthy patient could be subjected to any type of anæsthesia with satisfactory results, but that for the poor-risk patient the question of choice of anæsthetic might be very important.

Dr. HARRIS, in reply, said he considered the use of epidural anæsthesia to be unjustified. It was a method fraught with danger from the risk of injecting a heavy dose of procaine directly into the spinal canal, and had been superseded by intrathecal anæsthesia. He thought vinesthene a very suitable anæsthetic for the "chesty" elderly patient. Cardiac arrhythmia was a frequent complication of cyclopropane anæsthesia which on this account should not be regarded as non-toxic.

Advantages and Disadvantages of Intratracheal Anæsthesia

An occasional paper on this subject by Dr. ROSALIND P. MILNE and Dr. ROSS MACKENZIE, both of Aberdeen, was read by the former. The advantages of intratracheal anæsthesia and the conditions for which it was particularly suitable were reviewed. After operations for the repair of cleft palate she recommends that the tube should be left in situ for 12–24 hours—i.e., the period during which acute œdema of the glottis might occur. She considers that passage of a tube through the nose by the blind method might, if there was coughing and spasm occurred, cause damage to structures in the region of the larynx. In her opinion blind intubation should be reserved only for the rare cases in which use of the laryngoscope is contra-indicated. Even for oral surgery, oral intubation is favoured.

Dr. CHALLIS found blind intubation very satisfactory and safe. The possibility of causing damage with a laryngoscope must always be borne in mind.

Dr. GILLIES pointed out that the tube employed should be large enough to provide an adequate airway. If the tube were too small to allow free expansion of the lungs, pulmonary complications might result.

Dr. ROSS MACKENZIE replied that blind intubation should be reserved for the expert. The novice is not able to avoid the dangers inherent in this method and can be certain of passing the tube successfully only if a laryngoscope is used.

SECTION OF DISEASES OF CHILDREN

WITH Mr. GORDON BRUCE (Aberdeen) in the chair, this section discussed

Genito-urinary Infection in Childhood

Dr. WILFRED SHELDON (London) said that the work of Chown, and Wilson and Schloss showed that such infections were often blood-born, producing an interstitial suppurative nephritis rather than a pure pyelitis. Pyelonephritis was the more correct term and pyelitis seemed to be a misnomer. The essential point in diagnosing urinary infection was the finding of pus in the urine. What number of pus cells should be regarded as of pathological significance? Cumings and Alice Dickie had shown that urine from healthy boys usually contained no pus. The latter investigated the urine of 900 children free from urinary infection and found that, using a high-power lens, 50 per cent. of healthy girls had pus cells, up to two per field. Ordinary specimens of urine were used

after the vulvæ had been swabbed, a drop being taken from a shaken-up specimen.

Pyelonephritis was most common in infancy. Craig reported 61 instances in the neonatal period, while in Graham's series of 435 cases, more than half occurred during the first year. The sex-incidence was important. There was a preponderance of female cases but this applied to the period after infancy. During the first two years, boys were affected almost as frequently as girls, while in the new-born there was actually a preponderance of boys over girls. The high incidence of urinary infection in infancy had been ascribed to ascending infection through contact between soiled napkins and the vulvæ, but this argument was not valid since at this age there was no sex preponderance in girls. The probable cause was the commonness of gastro-enteritis at this time of life. There was often a history of bowel upset immediately before the onset of pyelonephritis. The infection was presumably blood-born and rigors at the onset indicated a septicæmic state.

The symptomatology of neonatal infection often differed from that in older children. The onset might be vague, with restlessness, vomiting, diarrhœa, pallor, collapse and pyrexia. The diagnosis of dehydration fever of the new-born should only be made after urinary infection had been excluded. Dehydration fever was relieved quickly by fluids, but the diuresis thus produced might equally well alleviate a urinary infection. Collapse attacks were alarming. In an infant a few days old, they should always suggest urinary infection. Vomiting was important, especially in more chronic cases. When an infant vomited repeatedly, passed unhealthy motions and failed to gain weight, urinary infection should always be thought of.

Breast-fed babies were almost exempt from pyelonephritis, and less prone to gastro-enteritis, scurvy and rickets. So vitamin deficiency might be a factor.

TREATMENT

In acute pyelonephritis alkalis were the remedy of choice. They sometimes caused slight diarrhœa in young children, but this was lessened if citrates and bicarbonates were used instead of citrates alone. Mandelic acid was an acid preparation and, for an acutely ill child with a high temperature, treatment with alkalis was on general grounds to be preferred. Alkalis would clear up cases only if uncomplicated by urinary-tract deformity. On the other hand, mandelic acid and sulphanilamide were likely to sterilise the urine even in the face of such deformity, hence one might be lulled into a false sense of security. If alkalis were used, full urinary investigation need only be carried out if there was no response to treatment. It was sometimes difficult to get the urine alkaline and it was essential to give alkalis by night as well as by day.

Chronic pyelitis called always for exclusion of congenital deformity. Full investigation should include culture of the urine, intravenous pyelography, cystoscopy and ascending pyelography. The latter was possible from birth in a female infant and in boys after the age of three years. Unilateral infection might be dealt with surgically. Alkalis, hexamine, vaccines and sera were generally without effect in chronic cases. Mandelic acid was effective with *Bacillus coli* and *Streptococcus fæcalis* but was of little use with staphylococci and *Bacillus proteus*. A concentration of 0·5–1·0 per cent. must be obtained and the pH of the urine must be at least 5·5. At the age of a year, 3 grammes of mandelic acid every 24 hours should be given. An extra acidifying agent was usually necessary, such as ammonium phosphate (15 to 60 grains according to the age of the patient and the methyl-red reaction of the urine). The sulphanilamide group were of definite value in chronic urinary infections. They were not effective against *Str. fæcalis* but would give prompt success in *B. coli* infections and would clear up that most resistant organism *B. proteus*. Sulphanilamide worked best in a slightly alkaline urine and should therefore be given with a small dose of alkali. Even in the face of renal damage, one was able to get a sufficient concentration in the urine. The dose of sulphanilamide varied with the age. For a baby half a tablet might be given 6 hourly. The dose at one year was half a tablet 4 hourly, while for older children it was one tablet every 4 hours. All the various preparations seemed to be equally effective.

SURGICAL TREATMENT

Mr. MATTHEW WHITE (Glasgow) said that organic lesions should, if possible, be dealt with surgically. In young children this was no easy task, and for this reason the high incidence of organic lesions had been overlooked in the past. In the literature figures as high as 40 per cent. were given. He had studied 125 chronic cases admitted for urinary investigation and 150 medical cases from the wards of Professor Fleming. The difference in age in the two series was striking. In the medical series the majority were under the age of two years, while many were under one. There were no cases in the surgical group under one year, the majority being over five. Medical cases were investigated chiefly by intravenous pyelography, but in surgical cases cystoscopy, catheterisation of ureters, and retrograde pyelograms were done.

The organic lesions found were hydronephrosis with or without obstruction, congenital deformities and renal calculi. In the medical series of 150 children, only two-thirds were subjected to intravenous pyelography, the others recovering so quickly that they were discharged. Organic lesions were found in 30 per cent. In the surgical series of 125 children, 65 had pyuria. Of these 27 or 41 per cent. showed organic lesions. The high incidence in boys (73 per cent.) was partly because stone was more common in male children. In the whole series, 18 cases had renal calculi but pyuria was present in only 8.

The commonest organic lesion was hydronephrosis. It varied from slight enlargement of one pelvis to gross dilatation of both sides. The origin was still obscure but two definite types could be recognised, one due to mechanical obstruction, usually congenital stenosis in some part of the urinary tract, and one without any obvious mechanical block. In the latter type, cystoscopy showed a large and patent ureteric opening. The hydronephrosis might be unilateral or bilateral. The origin was as yet obscure but some cases had in addition Hirschsprung's disease. There might be a neuromuscular disturbance responsible for both lesions. Satisfactory radiograms of the urinary tract might be obtained simply by running a solution of sodium iodide into the bladder.

DISCUSSION

Dr. H. G. OGILVIE (Newcastle-on-Tyne) was absent, so his paper was read by the honorary secretary of the section. In the cases under his care in the Babies' Hospital the majority had urinary infection as the sole lesion, but in over one-third it was part of a general sepsis. The onset was often acute with

violent vomiting, pyrexia, convulsions, refusal of food and development of the "gastro-enteritis syndrome." In other cases the onset was more insidious, the infant becoming fretful, drowsy and losing weight. In these cases there was a peculiar earthy tint of the skin which often gave a clue to the diagnosis. Acute abdominal pain, especially in older children, might lead to the diagnosis of acute appendicitis. Further, pus might not be present in the urine during the first few days. In treatment he found potassium citrate in infants did not give good results. It often caused gastro-intestinal upset. Sulphanilamide, and especially M. & B. 693, were much more satisfactory. In renal tuberculosis symptoms were often absent and the general health fairly good. Tuberculous cystitis was invariably secondary to renal tuberculosis. The prognosis should be guarded. Even after a successful nephrectomy, blood-stream infection might occur with a terminal meningitis.

Dr. ALAN MONCRIEFF (London) said that among 300 cases of dehydration fever under his care at Queen Charlotte's Hospital, the relief was so rapid when these infants were given fluid that he could not believe that the fever was caused by urinary infection or pyelitis. In urinary infection a recurrence might be brought about by insufficient fluid intake, the injudicious use of purgatives and upper respiratory infection. Acute *B. coli* fever was like typhoid fever and sometimes the spleen was palpable. When hourly records of the reaction of the urine were kept there was no correlation between the alkalinity and the fall in temperature.

Dr. K. H. TALLERMAN (London) said that it was his practice to give ½–1 oz. of fluid before each breast feed during the first few days of life. This had reduced the incidence of pyrexia in the neonatal period. Dehydration fever was particularly liable to occur in large infants who, because of their size, got insufficient fluid. He agreed that dehydration fever was not due to urinary infection.

Prof. G. B. FLEMING (Glasgow) stressed the importance of urinary stasis and referred to the high incidence of gastro-enteritis in urinary infection. He was convinced that in older children the lesion was often simple cystitis which cleared up with alkalis in a very short time.

Dr. FRANCIS ALLEN (London) said that a sustained temperature in the neonatal period often meant pyuria, and if frequent catheter specimens of urine were examined, it was surprising how often a *B. coli* infection would be found. In cases with chronic pyuria, repeated attacks might be secondary to an infection elsewhere, such as the respiratory tract. Dr. JOHN CRAIG (Aberdeen) drew attention to the initial septicæmia and to its connexion with acute bowel infections.

In reply, Dr. SHELDON said he was sorry if he gave the impression that dehydration fever was not a definite clinical entity. The point was that one should be careful in making such a diagnosis. Fluid would relieve the pyrexia, but in an infant with a raised temperature for 3 to 4 days, it was unsafe to make a diagnosis of dehydration fever. The cause was then usually to be found in the urine.

The Physically Subnormal Child

Dr. ERIC DOTT (Edinburgh) said his conclusions were based on a group of 70 children seen at the outpatient department of the Royal Edinburgh Hospital of Sick Children who showed a slightly subnormal physical constitution. These children became too easily fatigued when facing the wear and tear of ordinary home and school life. They presented many and varying symptoms of fatigue, including digestive, circulatory and nervous upsets. They were handicapped at school and were repeatedly under treatment for various complaints. The recurring symptoms caused much anxiety, both in parents and child. The important point in management was that there should be an endeavour to assess these children's capacity and to adjust their activities so as to avoid fatigue. This guidance and control had to extend over several years and periodical adjustment was necessary. Enough physical and mental rest was essential; if necessary school hours must be curtailed and hours of activity redistributed; diet must be adjusted to suit the child's digestive capacity and to include adequate fresh foods and vitamin B_1; a cheerful and confident atmosphere around the children must be aimed at. Full coöperation of parents and education authorities was essential. A regime of this nature had been applied in the 70 children mentioned. The follow-up showed that symptoms of fatigue could be greatly lessened and a much happier life for child and parents could be obtained.

Child-psychiatry and Pædiatrics

Dr. ETHEL DUKES (London) put forward a plea for closer understanding between pædiatrics and child-psychiatry. The family doctor was often the first to be consulted for behaviour problems and other psychological disorders, and he could consider the patient as a whole and could fully evaluate its environment. It was also possible that various organic diseases in children might be but the organic end of functional disorder. Psychic conflict or tension might bring about a state of malassimilation and malnutrition in spite of an adequate diet. In the so-called problem children, nervous complaints and somatic disorders were prominent features; the family doctor and the pædiatrician were more nearly concerned in the first place. The family doctor should be able to diagnose and treat minor psychological disturbances, and often he was the only person who could bring about the necessary environmental changes. Just as the general practitioner and the pædiatrician should develop the psychological approach, so the child-psychiatrist should have experience of children's medicine and normal children before he commences his special training.

New Inventions

COLOSTOMY TRANSFIXION PIN

THE pin and cap here illustrated may be found useful by surgeons who employ this particular technique. It is handier and less liable to damage the blood-

supply of the extruded loop than a glass colostomy rod, while the use of a pair of artery forceps for the purpose has always been deprecated by the theatre sister.

It has been made for me in stainless steel by Down Bros. Ltd., of St. Thomas's Street, S.E.1.

T. B. MOUAT, F.R.C.S.

"... When a thing is old, broken, and useless, we throw it on the dust-heap, but when it is sufficiently old, sufficiently broken, and sufficiently useless, we give money for it, put it into a museum, and read papers over it which people come long distances to hear."—SAMUEL BUTLER in his note-books.

REVIEWS AND NOTICES OF BOOKS

Facts About Food

By S. HENNING BELFRAGE, M.D. Lond. London: Humphrey Milford, Oxford University Press. 1938. Pp. 177. 3*s*. 6*d*.

Food, Health, Vitamins

(8th ed.). By R. H. A. PLIMMER, D.Sc. Lond., professor of chemistry in the University of London at St. Thomas's Hospital; and VIOLET G. PLIMMER. London: Longmans, Green and Co. 1938. Pp. 233. 5*s*.

Food, Facts, and Diet Planning

By GRACE MACDONALD, B.Sc., F.R.I.P.H., head of the science department, College of Domestic Science, Atholl Crescent, Edinburgh. London: Macmillan and Co. 1938. Pp. 168. 3*s*.

Sun Diet

By T. H. SANDERSON-WELLS, M.D. Lond., F.R.C.S.E., consulting surgeon, Weymouth and District Hospital. London: John Bale, Sons and Curnow. 1939. Pp. 100. 5*s*.

WHY do people write books about food? Here are some possible reasons. A publisher has suggested it; a teacher feels he ought to be an author; authorship may be a step towards a post as a teacher. Those devoid of self-interest are perhaps suffering from a repressed complex which must express itself—in other words a *cacoethes scribendi*. We suggest that no-one should write a book on dietetics unless he has done some research in the subject, unless he knows his subject, both qualitatively and quantitatively, unless he has a sceptical but none the less commonsense type of mind, and finally unless he has outlived the intellectual sloppiness of youth.

Only one of these books successfully passes these tests. The first author fails to be quantitative. "Meat is a good source of vitamin B" he says on p. 87. He is inaccurate: "The *carrot* is a good source of vitamin D or its precursor carotene and also of vitamin A" (p. 101). And he is very vague. The third volume is also non-quantitative and gives no evidence that its author knows her subject. "Some of the amino acids of proteins are," she says, "more important than others and they must be joined up in the proper order" (p. 34). Chapter VI is headed "The Large Intestine a Laboratory of Disease." The fourth volume is dogma without backing. *Biblia abiblia*.

Professor and Mrs. Plimmer's book is now in its eighth edition and, like good wine, needs no bush to advertise it. It has obviously met a need. To so well established a friend, criticism must be a compliment. Do the Professor and his wife really intend the implication contained in this sentence on p. 3: "Incidentally cancer and diabetes, two scourges of civilisation, have increased proportionately to the sugar consumption"? And what are we to say of the statement that "Cow's milk and green vegetables are the chief sources of calcium" (p. 38)? Many fish (see McCance and Shipp and p. 216 of the book itself) are better sources of calcium than most green vegetables except spinach, and in spinach the calcium is unavailable because of the oxalate present. In considering the effect of canning upon vitamin C it would be fair to mention Miss Olliver's work. The footnote on p. 72 reads, "Lævo-rotating polarized light to the left." This does not help the layman and sets the teeth of a physical chemist on edge. The relatively large amounts of vitamin B_1 in pig products do not receive mention on p. 94. And on what grounds do the authors say that in boarding-schools there is a prevalence of constipation? Statistics please! In spite of these blemishes (and a certain air of crankiness) the book may be recommended to those who can sift chaff from wheat, or better, bran and germ from endosperm.

Genetics and the Clinician

By LINDSAY RIDE, M.A., B.M. Oxfd., professor of physiology, University of Hong-Kong. Bristol: John Wright and Sons. 1938. Pp. 146. 10*s*. 6*d*.

RECENT progress in the science of genetics has been made chiefly in the fields of experimental breeding and cytology. As it is impossible to conduct breeding experiments in man, our knowledge of human genetics has necessarily been gained by indirect methods. The familial incidence of certain physical and mental characteristics is observed to correspond generally with the ratios which we have learned to expect from animal and plant experiments. How far can the knowledge thus gained be applied to the prevention of human infirmities? Professor Ride gives a complete answer to this question in a well-written and instructive book. It is valuable for what it omits no less than for what it includes. The reader is introduced to the principles of mendelism as observed in the pea and to those of chromosome behaviour as illustrated by the fruit fly. Then, in chapters which deal with genetical ratios in human pedigrees, anthropological physiology and the inheritance of blood-groups, these data are applied to man. There is a final chapter describing possible methods of advancing the study of human genetics and the book ends with a useful glossary.

Professor Ride has the gift of lucid and forceful writing. He succeeds in making both intelligible and interesting such complicated processes as linkage and crossing over of genes, independent assortment of genetic character and the confusions which have arisen in the description of human blood-groups. If his recommendations as to the teaching of genetics in medical schools were carried out, this volume would well serve the purpose of a textbook for use in the preclinical period.

Physiotherapy in Medical Practice

By HUGH MORRIS, M.D. Belf., D.M.R.E., consulting radiologist to the Devon Royal Hospital, Buxton; radiologist to the Salford Royal Hospital and the Royal Manchester Children's Hospital. London: Edward Arnold and Co. 1939. Pp. 276. 12*s*. 6*d*.

Dr. Morris says that he writes for the practitioner who has no specialised knowledge of electrotherapy, and his exposition is clear enough for the beginner. The subject matter is necessarily condensed, but Dr. Morris has included an amazing amount of practical information. The only chapters that suffer from excessive compression are those on diathermy and ultraviolet treatment. In the former the value of diathermy in improving the circulation and aiding growth in paralysed limbs deserves to be mentioned, and in the latter the excellent results obtained in surgical tuberculosis are not sufficiently stressed, the contraindications and risks of treatment are merely indicated and the grave danger of submitting cases of active pulmonary tuberculosis to routine treatment are not sufficiently emphasised. The chapter on infrared treatment is an able summary of the present position, in which current fallacies have been avoided. The book deserves a place on the shelves of every practitioner and of every electrotherapeutic department.

THE LANCET

LONDON: SATURDAY, SEPTEMBER 16, 1939

SOMETHING BETTER

THOSE who followed the deliberations of the seventh International Genetics Congress, reported in more detail on p. 663, felt it had something of a symbolic significance. Five hundred and sixty delegates, representing thirty-three countries, had met to debate the contributions of forty fruitful years to the youngest of the biological sciences. Five hundred and sixty enthusiasts, no longer iconoclasts, were thinking in terms of pure botany and zoology, the age-old crafts of plant and animal breeding, and, not least, of the scientific betterment of man himself. They were men and women animated for a time by an international spirit. Their only racial distinction was a specially warm welcome for the contribution of a delegate from a country other than their own. In spite of the wishful thinking that has taken the place of observation and deduction in the all-highest medical circles of Germany, the papers of the German delegates were listened to with interest and appreciation. The congress had the benefit of their presence for a single day only before they were recalled.

Genetics is no longer a novelty, promising sudden revelations or revolutions in scientific thought; it has settled down as a well-established branch of biology with its own laws, principles, and technique. A biological science so well established must have a definite contribution to make to medical education and practice. The General Medical Council has recommended that special attention should be paid to genetics during the preclinical years, presumably because it helps the student to understand the transmission of hereditary abnormalities, and the part played by inborn predisposition in disease. To the average medical student, and for that matter to the average doctor, genetics is still an obscure and academic subject, quite unconnected with the wards and the outpatient departments. The proceedings of the congress showed clearly, for the first time, that there does exist a science of human and medical genetics, different from the genetics of the textbook and the laboratory. Unlike the drosophila or the guineapig the human species cannot be artificially mated and it would need a Methuselah to follow out the effects of human mating. Instead one has to observe conjunctions apparently made at random. The problems presented are quite straightforward, but are not set out in the usual textbook form. Special mathematical methods are required. It is, however, fortunate that while the precise methods of computation may be intricate, and not as yet fully agreed upon, what the mathematician is trying to do is obvious enough. It could in fact be explained in the wards far more easily than many a problem in practical bacteriology.

Medical genetics is really a part of general medicine, with applications to the other clinical subjects, and not least to preventive medicine. The ideal is for the student to receive practical teaching in genetics during his ordinary instruction in the wards and special departments. A case of hereditary disease or abnormality might form the text for a discussion which would start with a reminder of the basic principles of the subject, and then apply these principles to the individual patient, the family group, and the population at large. Two of the special departments, the ophthalmological and the dermatological, get more than their share of hereditary abnormalities, and they might well serve as reservoirs of teaching material. When medical education once more settles down to an ordered routine, it would be a reminder that after war comes peace and rebuilding, if a few clinical lectures on genetics illustrated by patients, could be squeezed in. Genetics may seem a luxury in war-time. It takes many years to grow a man. It is quicker to kill him than to cut down a tree. In our preoccupation with destruction, genetics reminds us that the only justification for slaughter is a determination to build something better in its place.

CLOSED METHOD OF TREATING WAR WOUNDS

SINCE 1918 war surgery has not stood still, but has marched on, as it were, in mufti. Although great advances were made in the treatment of wounds and fractures during the last war, perfection was still far distant when it ended. The subsequent years of comparative peace have provided an opportunity for consolidating the positions reached and for further developing methods that were being evolved. For example, the one devised by WINNETT ORR for the treatment of infected open fractures has been applied to the treatment of osteomyelitis and is now widely used with various modifications. On a smaller scale the possibilities of what is known as maggot therapy have been explored, as is recalled by a letter in our correspondence columns this week. Recently, too, the war in Spain has given surgeons the opportunity for testing new methods in circumstances that presumably resemble those we may expect to meet in the coming months or years. Dr. JOSEP TRUETA had 2½ years' experience of surgery in Barcelona during the Spanish war, and valuable lessons may be learnt by considering the technique he evolved for the treatment of war wounds and fractures. This technique, already described in our columns,[1] is set out in more detail and with some interesting photographs in a small book published last week.[2]

What are the theoretical requirements for a

1. Trueta, J., *Lancet*, 1939, **1**, 1452.
2. Treatment of War Wounds and Fractures. By J. Trueta, M.D., late director of the department of surgery, General Hospital of Catalunya, Barcelona. London: Hamish Hamilton Medical Books. 1939. Pp. 143. 8s. 6*d*.

system of treating war wounds and particularly those sustained in air-raid casualties? A standard method that can be adapted to a great variety of injuries is desirable: it must deal with the results of both trauma and infection; it must be rapid; the instruments and apparatus used should be simple and few; the injured part should be immobilised in such a way that the patient can be transported away from the danger-zone as comfortably and as soon as possible; and a minimum of nursing and dressing should be necessary. TRUETA'S system fulfils most of these requirements. His first step consists in "débridement" of the wound, which is a thorough excision of all contaminated and damaged tissue, especially muscle, together with the removal of all foreign bodies (unless they are inaccessible) and the opening up of adjacent cellular spaces. Any associated fracture is then reduced, the wound is firmly packed with dry sterile gauze, and the limb is encased in plaster-of-paris which, in the absence of complications, is left in place for two or three weeks; only in exceptional cases is the wound sutured. It will be observed that no part of this system is in itself original; débridement is now generally practised although it is often followed by primary suture, and to pack the wound and encase the limb in plaster is simply to apply to recent wounds WINNETT ORR'S method for treating infected fractures. The result is a method of treating wounds and fractures that is certainly simple and fairly speedy. It can be adapted to many different sorts of injury, and it requires no special apparatus. The aim is to prevent infection, but if infection develops it remains localised and, so far as the body is concerned, external. The broken limb is immobilised and the patient is in ideal condition for being transported. The wound requires no further attention for two or three weeks. Last but not least, the treatment appears to be successful in saving both life and limb. TRUETA claims 90 per cent. good results and only 0·5 per cent. deaths in over a thousand cases of open fractures.

This so-called "closed method" has, however, several serious disadvantages. Perhaps the most important is that the progress of the wound cannot be watched. Serious complications such as gas-gangrene may develop under the plaster, and consequently they may be diagnosed and treated too late. TRUETA'S answer is that such complications seldom arise if the débridement has been skilful and thorough, and that when they do occur they can usually be diagnosed, or at least strongly suspected, without inspection of the wound. Danger-signals are deterioration of the patient's general condition, a rapid pulse, local pain, and œdema of the extremity beyond the plaster; in these circumstances the plaster should be at once removed. But this answer is not altogether satisfactory. It may be hard enough to diagnose early gas-gangrene when one has all available evidence, local and general; how much more difficult will it be when the wound is encased in plaster. And to remove the plaster in every slightly suspicious case would be to waste much time and often to interfere unnecessarily. Presumably it is only after much experience of this technique that the surgeon learns to interpret correctly the early signs of serious complications. Another big disadvantage is the stink, which sooner or later becomes intolerable both to the patient and those near him. Apart from general ventilation, no effective counter-measure has yet been devised except to change the plaster and the packing, and to do this frequently defeats one of the most important objects—namely, uninterrupted rest. A further difficulty that will sometimes be encountered is that plaster-of-paris is far less effective than continuous traction in controlling deformity in those fractures in which there is shortening maintained by muscular spasm. Despite these faults, however, it is obvious that this method has much to recommend it, and we believe it should be seriously considered by those now responsible for the treatment of air-raid casualties.

WHERE CELL TOUCHES PLASMA

THE combined surface of all the red blood-cells in the body is said to be about 3,000 square metres, and its importance in respiratory exchange is obvious. On another page Professor FAHRAEUS of Uppsala presents it to us in a new light as something intimately concerned with the life and behaviour of the erythrocyte itself. It is not, however, the exclusive property of the cells; it belongs equally to the plasma and is more correctly designated by the term "interface." Its dual significance is proved by the fact that when it is removed, as by segregating corpuscles and plasma, changes occur in both. The physical and chemical nature of these changes is unknown, but they both reduce the agglutination and sedimentation time of the red cells and reinforce each other. FAHRAEUS and his colleagues have devoted their attention chiefly to the alteration in the plasma; they postulate the formation, by an enzymic process, of a lecithin derivative similar to that found in cobra venom. Having formed spontaneously in separated plasma, the substance can be removed by suspending erythrocytes for a time in the plasma, and it is therefore held to be adsorbed on to the surface of the cells. The cells, besides losing their tendency to form rouleaux (and thus to sediment), then become more spherical, this deformity being associated with an increased tendency to hæmolysis. Since erythrocytes which have been separated for some time tend spontaneously to the same end, and since the spleen is a place where such separation occurs, a plausible theory of blood-cell destruction at once emerges, and is supported, as FAHRAEUS points out in his review, by evidence of increased susceptibility to hæmolysis of cells thrown into the circulation from the splenic stores.

Until all the factors have been thoroughly worked out, the theory must lack precise formulation, but of the significance of the work on which it rests there can be no doubt. The experiments have the simplicity of genius. It is abundantly clear even at this stage that they will ultimately throw light on many pathological, and it may be on

some metabolic processes. The evolution of the research is a striking example of the way in which work in one field will dovetail into that in another, apparently unrelated. Not content with his now familiar observation that the sedimentation rate of the blood-cells is greatly increased in pregnancy and certain pathological conditions, FAHRAEUS established agglutination as the cause and examined the various factors controlling this. They are numerous, and among the chief seem to be the concentration of globulin and fibrinogen in the plasma; these substances, it is suggested, tend to neutralise the negative electrostatic charge carried by the corpuscles which normally maintains them in a state of mutual repulsion.

One of the most fruitful lines of inquiry was the relation of stasis to agglutination, leading directly to an appreciation of the important of BARCROFT'S work on the reservoir function of the spleen and its possible physiological association with pre-hæmolytic changes. KNISELY'S analysis of the splenic circulation suggested to FAHRAEUS'S quick mind that since stasis must be associated with a reduction of the erythrocyte-plasma interface, this surface change and not the mere lack of mobility might be determining corpuscular deterioration. Put to the test, this inspiration proved to be well founded and led on to the possible solution of other problems. FAHRAEUS suggests that reduction of the interface may not be a local affair concerning only the spleen, where a special mechanism operates to separate the cells from the plasma, but may be significant in conditions such as anæmia and those in which rouleaux-formation occurs in the general circulation. To the uninitiated it might seem that this condition would tend to correct itself, since one of the signs of corpuscular damage is a diminished tendency to agglutinate, but FAHRAEUS thinks this tendency is masked by the powerful agglutinating influence of such factors as increased globulin concentration. His experiments certainly make it probable that the anti-agglutinative properties conferred by plasma-separation are by no means negligible, and must lead us to inquire how far the spleen contributes to the normal suspension stability of the blood.

ANNOTATIONS

DIAGNOSIS OF SHOCK

AT the present time the early diagnosis of shock is of the highest importance, for it is only in the early stages of shock that treatment is of any value. Now that blood-transfusion services have been organised it has become more necessary than ever to differentiate between hæmorrhage, which requires transfusion, and shock, in which there is already an excessive concentration of the red cells. On another page Mr. Layton suggests some guides to practice in dealing with abdominal wounds. Moon,[1] from published observations and his own experiments, demonstrates that the earliest sign of impending shock is a rising concentration of the blood as revealed by hæmoglobin estimation, by red-cell counts and by determination of the specific gravity of the blood. Hæmoconcentration often takes place even when the blood-pressure is *rising*; but if this happens a subsequent (possibly fatal) fall in blood-pressure can be prophesied with certainty. In hæmorrhage, on the other hand, a mechanism is at work which tends to restore the blood-volume to normal by absorption into the circulation of tissue fluids; this results in dilution of the blood and falling hæmoglobin values and red-cell counts. A difficulty is encountered when shock and hæmorrhage coexist; here, owing to the loss of red cells the hæmoconcentration is comparatively slight in relation to the clinical signs of shock. A hæmoglobin estimation, though not considered as reliable as a red-cell count, is the quickest means of verifying the existence of excessive concentration of the blood, and treatment of the wounded can readily be based upon its result. Thus a falling hæmoglobin indicates the need for blood-transfusion, whereas a rapidly rising value shows the need for anti-shock measures such as "forced fluids" by mouth or rectum. Plasma transfusion—an attempt to maintain the plasma volume, and a more or less stationary hæmoglobin percentage, in the presence of obvious clinical signs of shock—represents a combination of the two forms of treatment.

1. Moon, V. H., *Ann. Surg.* August, 1939, p. 260.

PROGNOSIS IN PREMATURITY

THERE are many difficulties in any large-scale follow-up study of prematurely born children, not the least of which is the tendency of parents to move house after an increase in family, especially when this is the result of a first-born. R. S. Illingworth has surmounted this difficulty however in an ingenious fashion, relying upon the well-known memory of mothers for the birth-weight of their offspring. He has kept records of 152 consecutive children above the age of one year who at birth weighed 5½ pounds or less, irrespective of the alleged duration of gestation, and compared them with similar records of 152 consecutive children who at birth weighed 8½ pounds or more. The children were attending the outpatient department of the Hospital for Sick Children, Great Ormond Street, for a wide variety of ailments; all, irrespective of ailment, were included in the series except for four, two in each group, who were suffering from such a gross defect as to make their inclusion unprofitable. Illingworth records[1] the results of his studies in various ways, the most important being concerned with the effect of birth-weight upon the weight chart. Previous studies had suggested that the weight curve of prematurely born infants tended to catch up to the normal at about the age of four years. Illingworth finds, however, that in his series 86 per cent. of all the premature infants were underweight at all ages (1 to 12) and only one child in the whole series of 150 fell into the 5 pounds or more overweight group. Actually the control series showed 34 per cent. underweight but most of these were within 5 pounds of the normal, whereas over 21 per cent. of the premature series were 10 pounds or more underweight as compared with 1·33 per cent. of the control series. Illingworth concludes that prematurity must be considered as a common cause of dwarfing and that weight charts which do not take into consideration the birth-weight are useless for dealing with the expected weight of any individual child.

Another comparison made was concerned with the

1. *Arch. Dis. Childh.* 1939, **14**, 121.

incidence of infectious diseases in the two series, since it might be expected that the premature child, being more "delicate," would be more liable to infection than the child of normal weight at birth. Actually he found no difference in the incidence of the infectious fevers in any of the age-groups examined. With regard to evidence of cerebral defect however the prematurely born (or, more strictly, the underweight) infant scores badly. The incidence of spasticity, mental deficiency and athetosis was compared in the two series and found to be much higher in the underweight group. Gross mental defect, fits or athetosis were present in 20 per cent. of the premature group as compared with 6·7 per cent. of the control group. Obviously this must not be interpreted as applying to premature infants in general, since Illingworth is dealing with patients brought to hospital because of some disease or defect, but the fact that evidence of cerebral defect is present three times more often among the infants who were small at birth contains food for thought for the obstetrician. A further finding showed an opposite result, so to speak, for the figures for asthma showed that there were nine times as many cases in the control group as in the premature group; and in a small series of cases of infantile eczema also examined only one out of fifty had been below 5½ pounds in weight at birth.

It is clear that there are many factors which may contribute to a low birth-weight—financial status of the mother, her diet during pregnancy, hereditary factors and pathological states of pregnancy—and certain of the findings in Illingworth's study may be related to other causes than mere smallness of size at birth. His work should stimulate those with access to similar records, for example among the well children attending welfare clinics or among the records of the school medical service, to sort out some of the points still requiring elucidation. The mortality-rate among premature babies is appallingly high: would its reduction mean the saving of a group of weaklings? Illingworth has supplied some of the answer, but we want to know the rest.

GERMAN MEDICINE IN THE LAST WAR

Prof. A. Waldmann was head of the army medical service on the German side during the years 1914–18 and it may be of interest to look at the achievements of this service through his eyes. Five years ago, fearing that the events of twenty years earlier were becoming unreal and almost legendary in the minds of the younger generation, he promoted a special number of the Munich medical journal[1] dealing with every aspect of military medicine and himself contributing a foreword. He tells us that of the 26,292 military doctors 1783 (6·8 per cent.) lost their lives, the proportion naturally being highest (10 per cent.) among the doctors at the front. They handled in all 27 million wounds and illnesses, of which 98·4 per cent. survived and 95·8 per cent. became again fit for service. These convalescents numbered on the average 67,000 men a month, or almost one half of the supply of fighting material. Waldmann estimates that the new hygiene and surgery kept alive a quarter of a million men who would otherwise have been lost. Actually some 40 per cent. of the men in the field were at no time ill or seriously wounded. The mortality from wounds was ten times that from disease and he contrasts this proportion with that of 5 to 1 in the Franco-German war and 1 to 6·5 (note the reversal) in the earlier wars of the nineteenth century. On the western front the incidence of typhoid was seven times less in 1914–18 than 1870–71 and a quarter as fatal. Smallpox and cholera had no footing, their place being taken by infectious jaundice, five-day fever, and trench nephritis; and he remarks on the curious fact that not only did diabetes and gout disappear "for the duration" but also scarlet fever. Venereal disease never reached its peace-time figure and was only 7 per cent. in the whole army. Experience gained in gas warfare had found useful application in industry and sanitation, and finally life in the field was the basis of a life lived closer to nature among the growing generation and had given birth to a new specialty of sport medicine. Waldmann concludes with the remark: "Military medicine also, by its fruitful contribution to medicine as a whole, obeys the law that war, in the sense of necessity, is the father of progress in human endeavour."

1. *Münch. med. Wsch.* 1934, **81**, 1157.

EXPERIMENTAL CANCER OF THE LUNGS

THE apparent rise in the incidence of human lung cancer makes it imperative to follow all clues available from experimental work concerning its cause. Although the rise cannot yet be satisfactorily explained, a number of relevant facts have come to light. It is now known that lung adenomata are the commonest of all spontaneous tumours in mice, that all stocks are afflicted to a greater or less extent, especially as the individuals grow old, and that a susceptibility is inherited as a mendelian dominant. All experimental observations have to be interpreted in the light of this knowledge. It has also been found that the incidence of these adenomata can be raised by the application of tar, or pure chemical carcinogenic substances, to the skin of mice, without necessarily producing a skin tumour at the same time; that is to say, the tumorigenic effect is seen in an organ remote from the point of application. This might indicate that, in seeking the cause of the human lesion, carcinogenic substances should be suspected in sources other than those that can reach the lungs with air—for example, in skin creams that are used regularly. Some doubt has now been thrown on such an interpretation, however, by an experiment recorded by Magnus.[1] In an attempt to produce gastric carcinoma in mice by injecting 1 : 2 : 5 : 6-dibenzanthracene, dissolved in olive oil, through an ingenious adaptation of the stomach-tube, he succeeded unexpectedly in raising the incidence of lung adenomata of his market stock from about 4–8 per cent. to 95 per cent., without producing any neoplasms in the stomach. More unexpected still was the unusual finding that 75 per cent. of these adenomata became malignant. The conclusion might have been drawn that here was another instance of a carcinogenic agent acting on the lung from a distance. Magnus, however, went on to test this supposition. He delivered similar meals, some containing charcoal and some containing carmine, into the stomachs of mice, and on killing the animals at successive intervals found coloured particles in the smaller bronchi and alveoli. This makes him think that in the previous experiment, despite absence of trauma, very minute quantities of the carcinogen accidentally reached and lodged in the respiratory tract. According to his calculation the total dose reaching the lungs in six months might have amounted to between 13 and 26 mg. It has already been suggested by Argyll Campbell[2] that when lung tumours follow painting of the skin with tar, the tar dries and flakes and is

1. Magnus, H. A., *J. Path. Bact.* 1939, **49**, 21.
2. Campbell, J. A., *Brit. J. exp. Path.* 1934, **15**, 287.

in fact inhaled as small particles by the mice. Campbell [3] has shown also that road dust with a content of only 2 per cent. of tar is capable of raising the lung-tumour rate from 8 to 80 per cent. when mice are subjected for long periods to an atmosphere containing it. The active agent in such a dust would probably be very dilute. It thus appears that by whatever route the carcinogenic agent reaches the lungs, whether directly with air or indirectly by the blood-stream, the effective dose may be extremely small.

COST OF MINIATURE RADIOGRAPHY

THE miniature radiogram as an adjunct to routine physical examination was mentioned in one of our leading articles a fortnight ago, in discussing the death of a militiaman from pulmonary tuberculosis a few weeks after being passed as fit. Now A. Robinson Thomas [4] has described in detail a simple set-up prepared for him by Watson and Sons of Parker Street, W.C.1. If ordinary 12 × 15 in. direct films were used, the outlay on examining 1000 men would be £100, since these films cost about 2*s*. each. Using 35 mm. film, nine photographs can be taken on 1 foot of film, and 16½ feet of this film cost 6*s*. 10*d*. at ordinary prices. Using miniature photography, therefore, the cost for 1000 men would be about £2 8*s*. The cost of the apparatus used by Mr. Thomas, including special developing tanks, screening stand, lightproof cone, miniature camera and lens, and also a special projector and screen, is about £650. As soon therefore as 7000 pictures have been taken, the capital expenditure on the new apparatus has been covered, and the enormous saving in running cost starts to show itself. The method is extremely rapid, and Holfelder in his clinic at Frankfurt A.M. claims to be able to examine 400 cases an hour. In Rio de Janeiro, de Abreu [5] is satisfied with 120 an hour. Berner [6] has already examined 55,666 patients of whom 32,360 were soldiers and 10,532 picked storm-troopers. Among the latter, 0·8 per cent. was found to have active tuberculosis, while among the German police, 1·68 per cent were found by the same method to be infected. In spite of mechanisation, personnel is still the most important thing in an army, and miniature radiography can scarcely be excluded from making its contribution to the health of our newly recruited forces on the grounds of expense.

THE SOUTH AFRICAN DOCTOR

ACCORDING to Dr. Dru Drury [7] there are three defects in the South African medical profession. Firstly there are too few doctors. There is one practising doctor for every thousand of the European population, but if coloured and native population are included, the ratio becomes one doctor for every five thousand. Secondly the distribution is faulty. One-fifth of the Union population live in nine large cities, but this fraction has attracted half of the available doctors. Cape Town has one doctor for every four hundred people, while the Transkei has one for thirty thousand natives. Lastly medical care is too expensive. White doctors fail to settle in native areas, yet Dr. Drury says that when the Rockefeller Foundation offered to found a medical school on the Rand for training native doctors the offer was turned down, and natives are not admitted to medical degrees in the existing universities. But of the need for a widening of medical practice the recent annual report of the M.O.H. for Cape Town leaves no doubt. He writes:

"The social and economic conditions of the Cape Coloured are on the whole unsatisfactory. The principle of compulsory education, which is applied to European children, does not extend to them; and although certain schooling facilities are available for them, in many cases of an inferior order, there is much illiteracy, and also a lack of discipline in certain classes of adolescents. With a very few exceptions they belong to the working class. A small proportion have skilled trades and receive satisfactory wages, but the majority belong to the unskilled labouring class. These receive very low wages, usually not more than 30*s*. a week when in full work, and often less. The wages of the head of the household are commonly eked out by the earnings of his wife and children. The City Council pays its labourers a minimum wage of £2 a week, but this is much above the local standard of wages. In the building trade the minimum wage for labourers is 9*d*. an hour. The resulting poverty produces its inevitable result amongst the coloured people. A large section of them suffer from malnutrition and their housing conditions are very bad. Alcoholism is common and there is a high incidence of venereal disease. The effects on their health are shown by the contrast between the vital statistics of Europeans and non-Europeans. . . ."

The racial distribution of sixth-year medical students in South Africa is interesting: Jews make up 37 per cent., English 33 per cent. and Afrikaans 26 per cent.

THE PROPOSED TUBERCULOSIS RESEARCH UNIT

EVER since the discovery of the tubercle bacillus attempts have been made to influence the course of tuberculosis by germicidal drugs—but always without appreciable result. Lately the success of surgical measures in cases proving refractory to regimen and diet has pushed the thought of chemotherapy into the background. The position is now changed by the advent of the sulphonamide group of drugs, although it would be unwise to argue that they must be effective in tuberculosis because they have given such brilliant results in other infections. But if chemotherapy is to find its place in tuberculosis it will surely be as a result of team work, the harmonious coöperation of bacteriologists, pathologists, biochemists and clinicians. For this reason we share the disappointment recently expressed in the *Times* at the decision of Middlesex county council not to adopt the proposal for a tuberculosis research unit. The council has, it seems, approved the principle, but holds the view that it should be a national rather than a local service. The proposal was to ask the Medical Research Council to second Dr. Leonard Colebrook, who is at present director of the research unit at Queen Charlotte's Hospital, to direct the new tuberculosis unit, bringing with him his own research team. The salary of the director would have been paid by the council, which would also have provided the raw materials of research from the Mill Hill laboratory. Although no results could be guaranteed, the establishment of a research unit such as that contemplated could hardly fail to yield information of therapeutic as well as of purely scientific value. The record of the unit at Queen Charlotte's has been remarkably good. We should like to see it made possible to achieve like results in another field. Preoccupation with more obvious foes can be no excuse for wavering in our offensive against Osler's captain of the men of death.

3. Campbell, *Ibid*, 1937, **18**, 215.
4. Thomas, A. R., *Public Health*, Sept. 1939, p. 347.
5. de Abreu, M., *Amer. J. Roentgenol.* 1939, **41**, 662.
6. Berner, F., *Röntgenpraxis*, 1939.
7. Dru Drury, E. G., public lecture to the twenty-third South African Medical Congress, July 10, 1939.

THE OTHER THIRTY-NINE MILLION

A LARGE proportion of the hospital beds of this country have been cleared for the reception of air-raid casualties, and a large proportion of the medical profession are waiting idle until these beds are filled. Meanwhile the size of the population has not diminished; there is as much illness as ever and in reception areas there is presumably more. The Minister of Health recognises this fact, and last April he said it was not proposed in war to keep the ordinary hospital service reduced below its normal level for any length of time; the Ministry, he told a Birmingham audience,[1] had in mind that the ordinary inflow of patients displaced at the outset of an emergency would in a few weeks accumulate again, and would require hospital treatment, and must be catered for. The difficulty arising here is that in a few weeks' time the emergency proper may not even have begun; and until a full attack has been made on our cities, and an equilibrium of forces has been established, we must expect the worst and must not relax our essential precautions. That brings up the question how far all the precautions are essential, and we submit that some revision is desirable even at this early stage. Is it absolutely necessary, for example, that London children, of whom perhaps half a million remain at home, should be turned away from the doors of our hospitals when there is an unoccupied staff inside that would gladly give them attention? We beg authorities, great and small, to permit the exercise of that gift for improvisation said to be one of the assets of our race. The medical service of the country is largely and inevitably dislocated; but it is *not* inevitable that consent should be withheld for the small efforts made by intelligent medical men and women to supply the needs around them. The requirements of the reception areas will be met in due course, we are assured, by the transfer of practitioners whose work has disappeared. Meanwhile we see obstetricians and pædiatricians, eating their heads off in rural hospitals, who are refused permission to start small informal child-welfare or antenatal clinics for the pregnant women and the children evacuated to the villages of the neighbourhood, with whom local doctors frankly cannot cope. The Ministry of Health cannot be expected, for the present, to investigate and expressly sanction small undertakings of this kind; but hospital authorities and medical officers of health will deserve no sympathy if they thwart initiative and strangle schemes that will help even a few of the many persons now deprived of the medical help to which they are accustomed. Nelson did not win by using his telescope to magnify the wording of the book of rules.

MEDICAL WOMEN IN THE SERVICES

THE actual number of medical women who served with the forces of the Crown in various capacities in the last war is not known, but it certainly amounted to many hundreds. They were employed on the staff of the Endell Street Hospital, in military hospitals at home and in Malta, Salonica and Egypt, and in the last year of the war with the Q.M.A.A.C., the W.R.N.S. and the W.R.A.F. These groups of women were recruited under different contracts and with different rates of pay and emoluments, so that women in one group never knew whether concessions made to other groups applied to them or not, and it was extremely difficult to take any combined action to improve conditions. The main disability from which serving medical women suffered was the lack of commissioned rank, which left them without authority over their subordinates and led to obstruction in their professional work and frequent humiliation. Those serving in military hospitals were not even allowed to wear uniform until March, 1918.

Further, however long and meritorious a woman's service might be she was not eligible for promotion, but was liable to be superseded by any newly joined officer, and she was also not eligible for many of the allowances given to her male colleagues. The refusal of the authorities to grant commissions to women was based on the view that they were not capable of performing all the tasks undertaken by medical officers, such as the command of field units and the inspection of recruits. The Medical Women's Federation argues, however, that this also applies to male specialists, and that although it was a good reason for limiting the number of medical women employed in war service the utility of women would be no less if they were given commissions. In March of last year the Federation stated their case in a memorandum[1] to the Secretary of State for War, and in July Mr. Hore-Belisha replied that "if a woman doctor be employed on military work it is considered that she would be given a grading which would rank with officers of the Army." Unfortunately this vague answer does little to settle the questions of rank, promotion, pay and allowances, uniform and the like which gave trouble before, and requests for further information have apparently been unheeded. In this war it may be some time before medical women are employed in military hospitals, but they will undoubtedly soon be attached to the corps of women working with the Army, Navy and Air Force. There are many problems connected with the hygiene and medical care of large bodies of women in camps and hostels which can only be dealt with suitably by doctors of their own sex. As things stand there is no guarantee that women doctors employed in the Services will have any more definite status than they had in the last war. The conditions of employment should this time be categorically set out as they are in the case of men, so that women may have an opportunity of considering them in detail before accepting them.

A MEDICAL LINK WITH SHAKESPEARE

IN 1607 Shakespeare's elder daughter Susanna married John Hall, a physician. Recent investigations have identified him with the John Hall, son of William Hall of Acton, who matriculated at Queen's College, Cambridge, in 1589, and proceeded to M.A. in 1597. He then went to France to study medicine, and eventually settled in Stratford, possibly as early as 1600. The master of Jesus, in a delightful little volume,[1] has put together a series of apparently unrelated facts which throw a little light on this somewhat obscure personage. He never took a degree in medicine at Cambridge and what induced him to settle at Stratford is unknown. But the master, who can build a pyramid on its apex as well as another man, surmises that his choice may have been due to the connexion of the Lucy family of Charlecote with some property in Bedfordshire which either adjoined that of the Halls or was actually owned by William Hall, the father of John. Further surmises make John Hall the source of certain names in Shakespeare's text, for example that of Dr. Caius, and certain phrases peculiar to Cambridge, also of the French in The Merry Wives and Henry V. But surmises apart John Hall physician emerges from the skilful reconstruction of the master as something more than a mere nominis umbra.

1. *Lancet*, 1939, **1**, 795.

1. Published in the Federation's *Quarterly Review* for July, 1939, p. 47.

2. Shakespeare's Son-in-law, John Hall. By Arthur Gray, master of Jesus College, Cambridge. Cambridge: W. Heffer and Sons. 1939. Pp. 22. 2*s*. 6*d*.

SPECIAL ARTICLES

TREATMENT OF INOPERABLE ABDOMINAL WOUNDS

By T. B. Layton, D.S.O., M.S. Lond.

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When it has been decided not to operate on a patient with a wound of the abdomen, with or without involvement of the chest, treatment consists of an inhibition of peristalsis, rest in the semi-erect position, and the supply of the necessary fluid to the body.

INHIBITION OF PERISTALSIS

The inhibition of peristalsis is obtained by giving nothing by the mouth and by the use of morphia. Abstention by the mouth must be absolute. It is not enough not to give food; no water or other fluid should be given. Anything put into the stomach causes reflex peristalsis. The only thing the patient needs to swallow is his own spittle; and there is not much of that. It should not be further diminished by the use of atropine, because the dry mouth is one of the things which require attention to secure rest; but only the irreducible amount of moisture to secure this may be introduced, and it should not be acid, for the smallest amount of acid sets up peristalsis. The moisture is better obtained by stimulation than by supply. Barley sugar may be used, or a flavoured glucose stick. It is well to allow the patient momentarily to suck this at short intervals and not to put a piece within the mouth. In this way relief of dryness is effected with a minimum of swallowed spittle. Alternatively the old-fashioned preparations of glycerin of borax or of honey of borax may be used, placing small quantities upon the tip of the tongue.

This absolute stoppage of all swallowing must be considered the main treatment. The inhibition of peristalsis obtained thereby is supplemented by the use of morphia by injection. This must be used freely and fearlessly; but it is important to remember that its use must be watched and studied. It is a weapon that must be used like a rapier and not as a neolithic club. To place a syringe and a phial of morphia in a registered medical man's hands no more makes him a doctor than to put a full-grained bat in a boy's hands makes him a Hobbs or a Grace. One of the most wonderful exhibitions in therapeutics that I have known was when an experienced physician kept a patient out of pain for a fortnight with tincture of opium in doses of 4-5 minims at intervals of four to six hours. And so it should be with the wound of the abdomen. At first a large dose may be given to ensure sleep after the mental strain. Then it should be the aim to keep the patient in a stuporose state just free from pain. This must be done by constant watching and judging. The dose and the interval must vary each time. It cannot be done by leaving routine doses to be given at stated intervals. The fear of producing a morphia addiction must not, at this stage, enter the mind. It is a fight for a life. When this is saved, there will be a prolonged convalescence in which any tendency to addiction may be eradicated.

REST IN THE SEMI-ERECT POSITION

The upright position was devised by Fowler in America. The idea was to drain any infective material within the abdominal cavity into the pelvis, where absorption is less there than it is from the region of the diaphragm and liver, and where the antibactericidal properties of the peritoneum were said to be greater. The position is, however, of as great value in wounds of the lung and in the bronchiolitis of influenza as it is in infective conditions of the abdomen; and with these lesions its value rests in the way in which the lowest and hindermost parts of the lung can become ventilated without undue muscular exertion. It is probable that this is as important in lesions of the abdomen as the drainage into the pelvis. The best position is not strictly upright. The body from the shoulders to the pelvis is at an angle of 45° with the horizontal and with the vertical. The hip, knee and ankle-joints being all flexed at right angles, the thigh, leg and foot are at the same angle in alternate directions.

In 1907 Lane, noticing that the patients tended to slip down in bed, put a pillow under the knees. To two of its corners he tied pieces of bandage, the other ends of which he fixed to the head of the bed. He thus anchored the pillow to the bed and prevented it from slipping towards the foot. In this way he retained the patient in the desired position. This is the origin of the appliance that subsequently became known as the Lane pillow. The improvisation is still invaluable when this pillow or other appliance, known as a "donkey," is not available. Without some such thing beneath the patient's knees no nurse ever has kept or ever will keep a patient in the desired position. The use of this appliance has, as a result of confusion of thought, fallen into disrepute of recent years. This is because it has been almost entirely used for patients upon whom non-infective civilian surgery, often gynæcological, has been performed; and a high proportion of cases of thrombosis of the veins in the pelvis has accompanied its use. This is not surprising. The surgeon has interfered with the circulation of this region by division of vessels and with his ligatures; and the patient, often middle-aged and stout, has remained in this position for three weeks. Further, in these cases the surgeon does not need the absolute rest that is essential to the patients under consideration in this paper. It is good for them to be moved from the very first and then with increasing range to move themselves. If, then, they slip down a bit they can be hauled up afresh by the lift of two skilled nurses. But when absolute rest is required, this repeated hauling exhausts the patient. When these patients have slipped down, it is distressing to see them. They lie on the lower part of the chest, so that with every inspiration the whole of the trunk has to be raised before any air can be drawn into the lower lobes of the lungs. Since the body cannot flex forward in the dorsal region, an acute bend develops in the cervical region, bringing the chin down and narrowing the upper opening of the chest, so that the jugular veins become compressed, and the retention of the blood in the head adds to the distress caused by its deficient oxygenation. Sometimes nurses become indignant when told that they cannot keep a patient in the desired position without the retaining pillow or appliance. They think it is a criticism of their personal skill. Fear of raising indignation in the heart of an individual nurse must not be allowed to endanger the recovery of the patient; for it is upon the absolute rest that this position ensures that, after the inhibition of peristalsis, the patient's chance of recovery depends. Its primary purpose is to prevent any infected fluids from trickling about the abdomen while the protective adhesions are forming; but it aids in that inhibition of peristalsis that has already been considered, and it is also a valuable factor in the treatment of shock.

Rest must be absolute. The nurse must for the time being give up all her routine with regard to the washing of the patient and attention to the skin. This specially applies to the back, where the development of bedsores must be risked. In this regard there is an advantage in the "donkey" beneath the knees. Without it the weight

of the body drives the pelvis down the bed, rucking up the upper part of the gluteal region with the area of the buttock, so that lesions tend to arise at the junction of the upper part of the gluteal region with the area of the sacro-iliac joint. With the "donkey" the contact comes upon the hinder surface of the upper parts of the thighs as far up as the gluteal fold, the pressure is more widely distributed.

In another respect also the "donkey" is conducive to rest. Many persons, especially in middle age, cannot rest comfortably with the knees extended. They must bend the knees, and to obtain the flexion they either roll sideways or flex the hips. Both of these cause movements, and the latter also cause the heels, on which sores may develop, to slip down the bed as the patient relaxes the muscles when dropping off to sleep. The result of this is that he wakes again with a jerk, and the much needed sleep is impaired.

The same principle applies to the head and neck. They must so be propped with pillows that the muscles of the neck are not in play to preserve the balance of the head. If they are, the moment the patient drops asleep these muscles will relax and the head flop sideways or forwards, waking him up again; or the head will bend backwards, and there he will fitfully sleep with the mouth open and suffer the more from dryness of the mouth when he awakes. The profound sleep, which helps recovery so much, depends largely on this position of the head. It is best for the neck to be slightly flexed. The patient does not want to stare at the ceiling. If the head is turned towards the entrance to the ward, he can open the eyes when anyone comes in and satisfy his curiosity without any movement. In this position also the nurse can get the necessary attention to the mouth without undue movement. If, however, the patient wants to, he should be allowed to move the head. If he is restless, he may be persuaded to keep the body quiet if he is allowed to move the head, and, if he will, the arms.

In the acquirement of absolute rest some patients may be hindered by their sensitiveness to noise. There are some persons whom any trivial sound keeps awake. For them the ear-plugs that are obtainable may make all the difference. Without them they stare wide-eyed round the ward; with them they sleep soundly.

SUPPLY OF FLUID

The third requisite in the treatment of an inoperable abdominal wound is the supply of fluid to the body. Primarily this is to prevent death from thirst; but it has its place in the treatment of shock.

The old distinction between shock and collapse is not made today; shock being the diminution of the difference between blood-pressure in the aorta and that in the venæ cavæ from a reflex disturbance due to excessive sensory stimulation, whereas collapse is a similar diminution due to the loss of fluid from the body or from its diversion into some part of the body from which it cannot be restored into the circulation. The important thing to remember is that with shock, as defined thus, time is a favourable factor once a decision has been made that nothing is to be done that will determine further shock. If an operation is imperative, there is a race against time to diminish the present in order to enable the patient to withstand the further shock of that operation. In the cases under consideration no such further shock from operation is anticipated. There is therefore no race against time.

The absolute cessation of further sensory stimuli that we call rest, combined with the application of heat, is the essential treatment of shock. Any attempt to hasten recovery may impede it. Every additional treatment of shock involves some disturbance which may do more harm than the treatment does good. There is no doubt that there have been patients whose chances of recovery have been destroyed by an excessive business in the treatment.

Judgment becomes still more difficult when, besides the shock, there is also collapse, as defined above. This may be due to loss of blood or to an exudation into the damaged tissues. When loss of blood has been excessive and has been stopped, it is advisable to replace the lost fluid at once. There is no quicker method of doing this than by the mouth; but, by the nature of the case, this route is interdicted and also it is not known whether the bleeding has been stopped or not, so that we are dependent entirely upon the natural arrest of hæmorrhage. Now, in its lesser degrees, shock is a part of this natural arrest. It is therefore undesirable to bring the patient out of the state of shock too rapidly. It is true that there is a further loss of fluid, not out of the body but out of the circulation in the form of exudation into the damaged tissues, as they swell up, and into its cavity, as the peritoneum becomes inflamed. This loss of fluid is, however, gradual. It does not need replacing rapidly. It must be forestalled by a slow but continuing supply. This is best given through the rectum; but, although the technical apparatus for its administration has advanced enormously, the question of how long and at what rate it can be administered has been forgotten. It is not generally recognised today that rectal infusion can be continued without cessation for a period of forty-eight hours or more at the rate of half a pint an hour. In 1907 nurses were doing this with an equipment which consisted of a piece of rubber tubing attached at one end to the nozzle of a Higginson's enema syringe and at the other to a bent piece of glass. The long arm of the bent glass went to the bottom of a pint measure containing saline, and this stood in a bowl containing hot water to keep the saline warm. The hot water was replaced from time to time and the saline refilled from hour to hour. The bowl stood upon the locker by the bedside, raised 12-18 in. above the level of the bed. What her mother did with this crude appliance thirty years ago the nurse of today can do with her modern apparatus, once she is told that it is possible and has it made clear that it is demanded of her.

LATER TREATMENT

The rest, the warmth, the morphia and the rectal infusion may be tried for six hours after the patient is in bed. If at the end of that time there is any improvement it may be continued. If the patient is barely holding his own or there is a set-back, then is the time to decide whether the saline is to be increased by injection into a vein or supplemented by transfusion of blood. And so the treatment should continue for three days. It is then that the absorption of twelve pints a day by the rectum may have begun to fail, and it is then that injection into the subcutaneous tissues either into the axilla with a needle through the pectoral muscle or into the submammary tissue may be of value. It is then also that the giving of food must be begun, and for this administration by the mouth is necessary. It still should be such that the peristalsis set up by it is minimal; and therefore anything containing extractives or a residue must be avoided, and it must not be hot. A thin gruel at body temperature with sugar added, or albumin water with some glucose may be used. The quantities given at first must be small. One way is to give a teaspoonful every minute for an hour by the clock, by which time the patient will have had some 8 oz. of the fluid. It is not necessary to have a trained nurse for this; a convalescent patient or a relation may do it; but it is necessary to have a watch, or too much will be given; and it is necessary to have the head slightly bent and turned to the side to

avoid any movement that will tire the patient by the frequent offerings of the spoon. After this time larger quantities may be given at longer intervals; but rules cannot be laid down, for the doctor and the nurse must feel their way. If this treatment be carried out, the nurse will never have to disturb the patient for from five days to a week, except for the passage of urine or possibly for the opening of the bowels, but this is likely not to occur if the peristalsis has been completely inhibited.

At the end of a week it will be known whether the patient is likely to recover or not; and the treatment becomes more active. But one thing is certain: at this stage he must not be moved.

HUMAN GENETICS

As noted by our Scottish correspondent on Sept. 2 the seventh International Genetics Congress opened in Edinburgh on Aug. 23. The papers covered an enormous range of subjects, but those dealing with human genetics will be of greatest interest to our readers.

Dr. I. LUNDHOLM (Ostersund, Sweden) discussed the *cause of hypochromic anæmia*. He said that as a result of his researches he had come to the conclusion that underlying the disease is a simple dominant gene, the effect of whose presence is to impair the absorption of iron from the intestine. In some persons the defect never becomes manifest, but if there is a loss of blood, anæmia follows owing to the slow absorption of iron. The regular loss of blood during menstruation amongst women or reproductive age is sufficient to produce the anæmia in bearers of the gene; it is therefore seen very largely among women aged between 15 and 50. Men who bear the gene do not suffer from the disease nearly so frequently; amongst those who do there is often a source of hæmorrhage such as an ulcer or hæmorrhoids. In some cases there is no apparent source of bleeding; it may be that in these persons the gene combines with such factors as lack of vitamins or infections.

In a session devoted to *statistical methods* in human genetics, it became clear that the refinement of mathematical techniques has proceeded very far. The difficulties inherent in the study of human material can be largely avoided if data are collected in systematic (but quite simple) ways, and if suitable methods for analysis are then employed. The contributors to this discussion were Prof. R. A. Fisher (London), Prof. J. B. S. Haldane (London), Prof. C. Gini (Rome), Prof. G. Dahlberg (Upsala), Prof. L. T. Hogben (Aberdeen).

Dr. D. P. MURPHY (Philadelphia) described an extensive investigation on the children of mothers who had produced a *congenitally malformed child*. The cases were obtained from death returns and represented, in all probability, a good random sample of such children. The chance that any subsequent child born to the mother would also be malformed was about one in eight, twelve times the expectation in the normal population. The commonest malformations were hydrocephalus, spina bifida and anencephalus. In sibships containing more than one malformed child the type of malformation was usually, but by no means always, the same in the affected sibs. Advanced maternal age was a factor of much importance.

Dr. BARBARA BURKS (Cold Spring Harbour) described genetic linkage between *hair-colour* and *deficiency in the number of teeth*. This has been demonstrated with a relatively high degree of probability and if finally confirmed will represent a notable landmark in the history of human genetics, for it is the first demonstration of linkage in any pair of chromosomes other than the sex chromosomes.

MENTAL DEFECT

Dr. T. A. MUNRO and Dr. L. S. PENROSE (Colchester) have found that *phenylketonuria* (inability to break down phenyl-alanine combined with low-grade mental deficiency) behaves as a simple recessive character. There is some evidence, inconclusive as yet, that this gene may reside upon the same chromosome pair as the ABO blood-groups. Dr. Munro, however, in answer to Professor Haldane (London) thought that it was premature to discuss this possibility further until more data are available. Dr. PENROSE stated that there was a genetic basis for *mongolism*, for a mongol child is ten times more likely to have a mongol relative than is a low-grade defective who is not a mongol. Maternal age is well recognised as an important factor in the ætiology of this condition, but it also plays a part in many others, including, for example, pyloric stenosis.

Dr. J. SANDERS (the Hague) described a family containing sixteen persons who suffered from *Pick's disease*[1]; this is the largest group yet recorded. The age at onset is about forty to fifty years, but it is possible that the application of mental tests may reveal the presence of the gene a considerable time before the disease becomes manifest. The disease depends upon a dominant gene, so that diagnosis amongst the children of affected persons is of much practical importance if marriage is contemplated. Up to the present the warning given by the mental-test results has been confirmed subsequently in three cases.

Dr. J. A. FRASER ROBERTS (Bristol) drew a distinction between *high- and low-grade defectives*. The former are part of the normal curve of variability of intelligence and, in so far as heredity is involved, owe their mental state to the operation of multi-factor inheritance. Low-grade mental deficiency may be of exogenous origin, but more often heredity is involved. The genes which cause low-grade deficiency are very numerous, each being responsible for a small proportion of cases only. They are sometimes genes which affect other bodily systems also. They include many genes which are expressed in a proportion of the bearers only. In many of these last cases, the other necessary predisposing factors must be prenatal. It is possible that such a gene makes its bearer unduly sensitive to minor variations which could not affect the development of the normal fœtus; trivial differences would then determine whether the central nervous system was affected or not in a particular bearer of the gene.

Dr. R. J. A. BERRY (Bristol) described an analysis of the mental characteristics of the *relatives* of a large group of *mental defectives*. The most striking finding was the notably higher proportion of affected children if a parent was also affected.

MENTAL ILLNESS

Prof. D. K. HENDERSON (Edinburgh) made a close analysis of eugenics in relation to *insanity*. He considered that both negative and positive eugenics were involved in a constructive programme, but emphasised that improvements of environmental conditions must also be regarded as essential to such a programme. It is easy to encourage too fatalistic a view of the hereditary determination of mental disease. He would not be prepared to sacrifice the members of families containing manic-depressive patients in order to reduce the incidence of the disease, for such people, who might well exhibit slight degrees of abnormality, often possessed qualities which were of value to the

1. Pre-senile dementia, *not* polyserositis.

community. While not ruling out sterilisation as a useful procedure in a few selected cases, Professor Henderson criticised the findings of the departmental committee on sterilisation (1933), in that the indications suggested were so vague. He also criticised the German plan because it was so sweeping and might interfere with early treatment.

Dr. F. J. KALLMANN (New York) stated that the inheritance of *schizophrenia* could be interpreted on the basis of a single recessive factor. This factor, however, was not always expressed and external circumstance may determine not only whether the bearer becomes affected or not, but also the features of the mental breakdown. He did not consider that sterilisation could play anything but an insignificant part in eradicating this disease.

BLOOD-GROUPS

In discussing *blood-groups*, Dr. V. FRIEDENREICH (Copenhagen) described the division of "A" into three varieties, distinguished by the strength of the reaction. A_1 is dominant to A_2 and A_3, and A_2 to A_3; A_3 is very rare, but the distinction between A_1 and A_2 is already employed medico-legally on the Continent, thereby increasing the proportion of cases in which false accusations of paternity can be disproved. An important piece of work by Dahr was mentioned. It is possible that persons of constitution AA may soon be distinguished from those of constitution AO. This would still further increase the usefulness of the blood-groups in medico-legal work. Dr. G. L. TAYLOR (London) issued an impressive warning in regard to the danger of error in MN blood-grouping. The sera may easily contain unwanted antibodies and so give false positive results, or by over-exhaustion be rendered too weak and so yield false negative results. Further the sera may quickly lose their potency. Statistical examination of much published data obtained from all over the world clearly shows that many such records must contain a proportion of false results. MN blood-grouping, especially of course in medico-legal work, is a procedure which should be left to serologists of experience.

Prof. R. RUGGLES GATES (London) discussed blood-groups from the anthropological point of view, and stated that while gene A probably arose in the common ancestors of anthropoid apes and man, gene B in all probability arose much later by parallel mutation in both stocks. Dr. D. J. FINNEY (Harpenden) produced evidence which indicated that allergic disease may be linked genetically to the ABO blood-groups (the genes being situated upon the same chromosome pair). This however requires further confirmation.

TUMOURS

Dr. ALMA HOWARD and Dr. C. L. HUSKINS (Montreal) have found that the incidence of *mammary cancer* in various strains of *mice* is associated with the chiasma frequency, that is, with the frequency with which crossing over occurs between the chromosome pairs at certain stages. Dr. MADGE T. MACKLIN (London, Canada) has analysed a series of human *twins* in which both members developed tumours. Some of the material was collected personally and some from the literature. Out of thirty-four pairs of identical twins thirty-two showed the same kind of tumour occurring in the same organ, while two had tumours of different kinds. Out of fifteen pairs of fraternal twins seven had the same type of tumour and eight dissimilar tumours. In cases in which the age at onset was known, the mean difference in the case of the identical pairs was 1·3 years and in the fraternal pairs 12·1 years.

ANIMAL EUTELEGENESIS

In the animal-breeding section a session was devoted to *artificial insemination*. This technique is now very widely used in agricultural practice throughout the world, and has attained a high degree of perfection in such animals as cattle and sheep. Dr. J. ANDERSON (Naivasha, Kenya) stated that the artificial insemination of cattle was especially valuable in Kenya owing to the prevalence of genital disease transmitted by coitus. About 12,000 cows per annum are now being inseminated. The farmers themselves carry out the technique after receiving instruction. In sheep the results are very nearly comparable to those obtained by natural methods. Dr. T. BONADONNA (Milan) stated that about a hundred centres were now at work in Italy and her colonies, some 80 per cent. of their activities being concerned with cattle. Other animals yield very successful results however; in sheep 80 to 90 per cent. of pregnancies result; in mares 70 to 80 per cent., if more than one insemination is made during the heat period; in sows 90 per cent.; and in hens 90 to 100 per cent. Dr. R. W. PHILLIPS and associates (Idaho, U.S.A.) have experimented with long-range *transportation of rams' semen* and have obtained pregnancies after transportation for 2600 miles. The longest interval between collection and successful insemination was 115 hours.

Dr. M. TEODOREANU (Bucharest) described particularly successful results in sheep, obtaining 96·5 per cent. of pregnancies, a figure equal to that of normal mating. Dr. J. EDWARDS and Dr. A. WALTON (Cambridge), who have been responsible for many advances in this field, described a careful investigation on factors controlling the fertilizing and storage properties of the semen of a group of bulls; further advances in technique may be anticipated in the near future.

Dr. M. MANRESA and associates (Philippine Islands) have conducted experiments since 1930 to determine why pure-bred cattle imported from countries of temperate climate should prove unsuited to the Philippine Islands. Imported cattle had a much lower hæmoglobin content in the blood than native cattle. This is interpreted as a temperature effect, for variations in external temperature were associated with blood variations in the imported animals, though not in the native ones. The body temperature of the imported cattle was consistently higher than in the native cattle. It is concluded that high temperature and high relative humidity raise the body temperature of the imported animals with serious effects on the physico-chemical balance of the blood. Cross-bred progeny proved to be intermediate.

A feature of the congress was the wealth of demonstrations and exhibits. Particular interest was aroused by the demonstration on blood-grouping and taste-testing (for the ability to taste phenyl-thiocarbamide) arranged by the Galton laboratory of the University of London. Many visitors were blood-grouped and taste-tested, and at the end of the congress members were invited to observe an attempt to test the taste reactions to this substance of the anthropoid apes at the Edinburgh zoo.

". . . 'There is no reason whatever to believe that the order of nature has any greater bias in favour of man than it had in favour of the ichthyosaur. . . . I perceive that now the universe is bored with him, is turning a hard face to him, and I see him being carried less and less intelligently and more and more rapidly . . . along the stream of fate to degradation, suffering and death.'"—H. G. WELLS, quoted in a review. *Nature, Lond.*, Sept. 2, 1939, p. 397.

THE MOTORISED FIELD AMBULANCE

IT is a well-known principle of warfare that whereas both sides begin a war with the tactical ideas of the last war but one, the medical arrangements are based on the last war but five or six. This cannot be said of the R.A.M.C. in "Hitler's War," since the modern field ambulance has been entirely motorised, whereas the whole R.A.M.C. at the beginning of the last war had at their disposal only seven motor-ambulance cars.[1] The questions now arise whether this mechanisation has gone far enough and whether it requires a radically altered organisation to make it fully effective. Lieut.-Colonel Dowse[2] suggests that the modern field ambulance may not have kept pace with the enormous mobility conferred by mechanisation on the fighting arms. He considers that, as now organised and equipped, it is not sufficiently mobile to carry out its primary duty of collecting and evacuating wounded, and that the present system of evacuation from the regimental aid post via the advanced dressing station to the main dressing station and thence by the motor ambulance column to the casualty clearing station is too cumbersome. In the first place, 48 of the personnel of the field ambulance cannot be seated in the vehicles of the unit, and this must seriously handicap its mobility. Secondly, Colonel Dowse maintains that the heavy ambulance is unsuitable for its purpose and that the number of motor ambulances in the forward area is inadequate.

The essential change that Colonel Dowse would like to see made is the abolition of the main dressing station. The surgeons say that 99 per cent. of wounded should be in their hands for treatment as soon as possible after they become casualties, irrespective (within limits) of the length of the journey. What then is the purpose of the main dressing station, at which little operating can be—or is in fact—performed? Its abolition, together with its bulky equipment now carried by the headquarters company of the field ambulance, would allow all the personnel of the field ambulance to have a seat in motor vehicles. The casualty clearing station, however, may be as much as 50 to 100 miles behind the forward troops, and therefore a forward operating centre of the C.C.S. will be required, as was being developed at the end of the last war. If cases are evacuated directly from the advanced dressing station to the casualty clearing station it is obvious that a great increase in the motor ambulances working in the forward areas will be necessary, and this would be obtained by absorbing most of the ambulances in the motor ambulance convoy into the "forward evacuating unit"—the name which Colonel Dowse suggests for his new organisation. There are two duties of the field ambulances which would have to be transferred to non-divisional medical units administered by the D.M.S. or D.D.M.S. of army or corps respectively: these are the tasks of establishing rest stations for sick and wounded who are likely to rejoin their units in a few days, and of gas centres for the special treatment of gas casualties. Neither of these organisations needs to be mobile and the transfer from division to corps or army would be an advantage rather than otherwise.

In view of its greater mobility, the present cavalry field ambulance seems to be nearer the ideal than the infantry field ambulance, but under the proposed organisation a single type of field ambulance will be suitable to work with all types of divisions, thus securing a desirable uniformity. Colonel Dowse would prefer to see a proportion of the light two-stretcher type of motor ambulance included in the forward evacuating unit, and he thinks that motor-cycle stretcher-carriers might be developed, as in the French army. The motor ambulances of the forward evacuating unit would consist of 20 heavy cars with H.Q., and 5 heavy, 10 light and 10 motor-cycle stretcher-carriers, or an additional 10 light cars, with each company, giving a total of 95 per division. As regards personnel, Colonel Dowse supports the suggestion that bearer officers—i.e., promoted N.C.O.s of the R.A.M.C.—should be in charge of the evacuation of the forward areas, thus releasing qualified medical men for more essential services.

Thus Colonel Dowse envisages a divisional field ambulance or forward evacuating unit of a uniform and highly mobile type, whose duties would be confined to establishing advanced dressing stations, collecting the wounded and dispatching them to the C.C.S. or its forward operating centre, to the rest station or to the gas centre. As has been well said, a field ambulance is doing its duty best when it is empty.

1. Official History of the War. Medical Services, vol. 1, p. 53.
2. *J. R.A.M.C.* June, 1938, p. 374.

SCOTLAND

(FROM OUR OWN CORRESPONDENT)

EDINBURGH IN WAR-TIME

ONE of the results of the medical A.R.P. organisation in Scottish cities is the temporary disappearance of the hospital population. In Edinburgh evacuation of the patients in the Royal Infirmary and the three municipal hospitals was carried out. The seriously ill patients were accommodated in convalescent homes, public assistance institutions and so on, but, whereas before the war nearly 3000 beds were occupied by persons presumably requiring hospitalisation, only about 300 are now occupied. The discharge of so many patients to their homes has thrown an enormous amount of work on the general practitioners at a time when their numbers are greatly reduced and many of them are hard at work on various A.R.P. duties. At the same time, the diagnostic services of the hospitals have stopped. In the efforts which have been made to cater for civilian casualties, medical services for those who happen to fall ill during the initial stages of war have been rather overlooked. Already, however, the situation is coming under control. In Edinburgh the public assistance institution is being rapidly converted into a general hospital and some of the beds in the Royal Infirmary are to be liberated from war purposes to supplement those which have so far been used for ordinary emergencies. The infirmary will continue to hold empty 1000 beds in readiness for air-raid casualties. In radiological departments, the more time-consuming and laborious barium examinations are to be restarted shortly. Needless to say, emergency radiology, of fractures and so on, has not ceased.

A.R.P. IN THE UNIVERSITIES

The dramatic changes which have overtaken other public buildings in the last few days have not passed by the universities. Apart from the sand-bagging of the more important parts, departmental staffs have been busy packing and placing in safe storage valuable apparatus, specimens and other teaching and research material. In Edinburgh continuous fire patrols of the university buildings are being organised, students

forming the personnel with members of the staff acting as leaders. The professorial staff has worked wonders in the rapid construction and equipment of first-aid posts and shelters. In the medical school, ground-floor rooms in the anatomy department and the rooms of the students' reading room have been protected and well equipped with the necessary running water, sterilisers, dressings, stretchers, &c., while a canteen for the aid-post team is rapidly being finished. The bowels of the earth are hollowed out into troglodyte shelters, into which, like threadworms in the appendix, everyone will crowd when the warbling sirens start.

EAST FORTUNE SANATORIUM

Some time ago the Air Ministry announced their intention to acquire the ground about East Fortune Sanatorium for use as a landing-ground. The sanatorium authorities objected that the existence of the sanatorium and a landing-ground were incompatible, and that the institution, which accommodates 211 patients and serves the whole of the south-east of Scotland, would have to be given up. It has now been announced, however, through Mr. George Mathers, M.P. for the Linlithgow division, that the Ministry have decided not to proceed with their scheme.

GRAINS AND SCRUPLES

Under this heading appear week by week the unfettered thoughts of doctors in various occupations. Each contributor is responsible for the section for a month; his name can be seen later in the half-yearly index

FROM D.P.M.

III

THE engineer deputed to reorganise my black curtains stood on the top of the ladder and delivered me a short address on Hitler. There was nothing strikingly new about it except that, in his opinion, Hitler was no leader. "I always say," he repeated, "that he's not a leader." I could think of no satisfactory reply to this, so he went on to tell me what his wife thought about the war; and here I found myself in my depth again, for his wife and I seem to share the same views.

"I've blacked out our bathroom light," he said earnestly, "so that we get one little beam on the mirror for me to shave by. My missus said to me: 'Is that all the light we're going to get, then?' I said, 'Yes, my girl, that's all, till the war's over!' 'Cor,' she says, 'no light, no pictures, and nothing but music on the wireless. What do they think we are?'"

What indeed? No-one can deny that the atmosphere of Victorian piety in which this war is being conducted has grown thicker and thicker during the past week. The niggardly crumbs of news doled out to us are no compensation for days which end at dusk, and nights spent in rooms muffled in black curtains and heated to the temperature of a moderate oven. Even threatened air-raids are so well supervised that the wretch going through the streets is hurried down some hole in the ground by an air warden before he has a chance to explain his phobia (supposing he has one) of being buried alive. All this paternal solicitude is very nice—but boring. Of course we should be grateful; we should be pleased to find ourselves safe, and to know that any news that might cause us a moment's uneasiness is being kept from us. Perverse and foolish, however, we are as restive as children under the thumb of a too solicitous nanny, the sort who insists interminably upon a body-belt and a dry pair of socks.

Surely we could be treated more successfully as adults? What objection could there have been, for instance, to giving us at once the text of those leaflets dropped over Germany by our airmen? Theirs was a splendid adventure, if ever there was one. Surely we deserved to hear that tale in full?

Is it just possible that this silence and organised gloom is part of a deep-laid scheme? Can it be that someone has at last realised that the way to make warfare universally and permanently unpopular is to make it boring? There is a strong strain of asceticism in mankind. Men and women will put up with unthinkable agony and grief if they believe it to be a good cause. On the other hand, no cause has yet been found to make boredom seem attractive. Or anyhow, to make it seem attractive to me and the engineer's wife, and I daresay there are plenty like us.

* * *

THIS question of boredom is very interesting. Boredom must often have been responsible for wars, though no-one could complain that boredom led up to this one. Bored children squabble; bored nations, perhaps, go to war. In the Middle Ages, it has been suggested, boredom led to witch-hunts. Among villagers isolated from any sort of entertainment a suspected witch must have been a godsend. Among the border clans a chief at his wits' end to occupy a body of highly trained and quarrelsome clansmen must have been thankful to suggest a raid on someone else's cattle. In these situations the change was from a static to an active phase, a loosing of chained energy.

But suppose we could reach a point where the reverse was the case, where the constructive activities of peace gave more outlet for our energy, skill and even our aggression, than the disciplines of war? Suppose war became the passive, boring phase, under which we fulminated to an uproarious and active peace? That would be a thing worth seeing. It would not necessarily mean the end of war, because human institutions are apt to be cyclic; there is a time for building up, we are told, and a time for breaking down. But it would mean that wars were brief and unpopular—dull interruptions of our more violent deeds.

* * *

The emergency medical arrangements appear to have been carried out with great speed and accuracy; hospitals have been cleared for casualties and important units moved out of the danger zone. It is pleasant to know that some of the hospitals are evacuating their younger nurses to outlying institutions. London may seem dull at the moment, but there is no guarantee that it will remain so. The seventeen- and eighteen-year-old nurses looking after London's mentally defective children are staying where they are with a very good grace.

One drawback to the emergency arrangements as they affect the civil population is beginning to show itself. A friend of mine in general practice tells me

that he sent a case of just-operable cancer to all the hospitals in his region, but could get no treatment for her. Many other doctors must have encountered similar difficulties. The status of the civilian in wartime is always rather mysterious. Presumably the army fights to protect the civilian, yet the civilian is always neglected in favour of the army. He gets worse food, worse medical care and worse gas-masks. It all seems very curious. Either the civilian is worth protecting—in which case he is worth preserving, too; or else he is not worth protecting—in which case, why keep an army? I can't make it out.

* * *

I suppose there are good reasons for training nurses to have blind faith in the doctor—except that I cannot suppose there is any really good reason for training anybody to have blind faith in anybody else. Sometimes the trust of the nurse is stimulating and sometimes embarrassing; and sometimes it makes one wonder what goes on in the nurse's mind. I have known a nurse refuse to admit she was looking after a case of pneumonia though she had been nursing the patient perfectly for a week, and had herself copied the word pneumonia on to the temperature chart in capital letters. She said that she didn't like to own she knew it was pneumonia for fear the doctor would think she was making a diagnosis.

I provoked one staggering exhibition of blind faith during the first air-raid warning. While I was waiting in one of the wards with a first-aid squad the telephone rang; the voice of my senior officer came briskly over the wire: "Fill the bath!" I turned to the nearest nurse—"Fill the bath," I said. "Yes, doctor," she replied breathlessly, bolting like a rabbit into the bathroom. A moment later her flushed and earnest face appeared round the bathroom door. "Hot or cold, doctor?" If the incalculable creature chose this moment for a dip, hers not to question, I suppose she felt. She put me in mind of Casabianca, whom I admire but cannot respect.

* * *

A minor pleasure of war is to be found in filling sandbags. Half the hospital turns out for this sport and prosecutes it with enthusiasm. I did not realise until instructed by the gardener—who looks like Lloyd George but is less loquacious—that there is an art in filling a sandbag. A full team consists of three: one to delve and one to hold and one to tie the sacks. They put me on to holding at first, that being the simplest job, but after a short trial Lloyd George shook his head and beckoned to one of our mental defectives to show me how it was done. It seems you have to hold the back lip of the sack firmly, with your hands about eight inches apart and the canvas taut between them; the front lip of the sack then sags forward, leaving space for the introduction of the shovel. It was some time before my performance satisfied the gardener. After that they let me dig a little, and here again there are points to be observed; a sack must not be filled too full or it refuses to lie flat when banked among its fellows; and the shovel—our shovels are nearly as wide as the mouths of the sacks—have to be introduced tenderly or half the load trickles out and is wasted. I discovered no special points about tieing except that it blisters the left little finger.

At first we filled the sacks from our meagre garden, with the result that some of them are now sprouting green blades and lending the wartime aspect of the hospital a hoary appearance already; later a fair portion of Clapham Common arrived on lorries and enthusiasm reached a high pitch. I think the children felt that Bognor Regis had come to town, and greeted us on the morning round with: "Doctor, can I fill sandbags? Can I fill sandbags, doctor?" Large and tireless parties gather on the imported dunes in every spare moment, using anything they can get, from seaside spades to ornamental fire-shovels; and the growing piles of sandbags lie round them looking like the malt sacks out of "This is the House that Jack Built." The padre who arrived hopefully to conduct a service was completely out of the running. "You tell him he can go home and pray for us, sister," the patients said kindly to the worried messenger.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED SEPT. 2, 1939

Notifications.—The following cases of infectious disease were notified during the week: Smallpox, 0; scarlet fever, 1035; diphtheria, 756; enteric fever, 77 (53 "expected"); pneumonia (primary or influenzal), 301; puerperal pyrexia, 149; cerebrospinal fever, 18; poliomyelitis, 21; polio-encephalitis, 1; encephalitis lethargica, 1; dysentery, 26; ophthalmia neonatorum, 28. No case of cholera, plague or typhus fever was notified during the week.

Deaths.—In 126 great towns, including London, there was no death from smallpox, 1 (0) from enteric fever, 2 (0) from measles, 3 (0) from scarlet fever, 8 (4) from whooping-cough, 14 (0) from diphtheria, 44 (6) from diarrhœa and enteritis under two years, and 8 (1) from influenza. The figures in parentheses are those for London itself.

Liverpool reported the only death from typhoid. Fatal cases of diphtheria were scattered over 12 great towns, South Shields and West Bromwich each reporting 2. Liverpool had 9 deaths from diarrhœa, Birmingham 6, Nottingham 5.

The number of stillbirths notified during the week was 234 (corresponding to a rate of 33 per 1000 total births), including 40 in London.

The Lancet 100 Years Ago

From an article on small-pox in Chelsea by Dr. W. B. Marshall

I CARE not to mingle the question of money with that of the public health; and am not, therefore, solicitous to suggest any mode of remuneration for the authorised vaccinators, but I may add that the cost of coffins alone, for small-pox patients, during the year ending April 30th, 1839, would, I am sure, have more than paid for the vaccination of every one who has been attacked with that disease during the same period; a clamour might, and, doubtless would, be raised against any law to that effect, upon its first introduction, but, like all senseless clamours, it would soon subside, and as the law came into operation, the benefits thereof would be better appreciated, and, of course, more cheerfully acceded to.

"... You shall always be told the truth in this war. Maybe that at the front there is a serious reverse—that shall not be hidden from you. If listening to foreign radio stations is heavily punished, it is not because we fear them, but because it is dishonourable to listen to the dirty tirades of foreign countries."—Field-Marshal GÖRING in a Berlin armament factory on Sept. 9.

"... You can drop a bomb somewhere but you can broadcast the truth everywhere."—Sir WALFORD DAVIES, quoting his taximan in a broadcast on Sunday evening, Sept. 10.

LETTERS TO THE EDITOR

RED CROSS AND ST. JOHN JOINT APPEAL

THE following letter, signed by the Duke of GLOUCESTER, Sir ARTHUR STANLEY and Lord SCARBROUGH, has been issued to the press by the Red Cross and St. John Emergency Committee.

In the grave issues which now confront the British Empire, the British Red Cross Society, of which H.M. the Queen is president, and the Order of St. John, have decided to work together as they did in the last war with results which are still within the memory of the public. With this object a Joint Emergency Committee has been set up, comprising an equal number of members of each body. Lord Cromer has consented to be the chairman of the committee with Major-General Sir John Kennedy as vice-chairman.

In this war, which is so entirely different from any that has preceded it, it is impossible to foresee exactly where relief for the sick and wounded will be most needed, or in what form. But it is certain that there will be vast suffering and distress and that the relief of the sick and wounded of His Majesty's forces, and of the civilian population, will call for much voluntary effort and financial support. Considerable voluntary help has already been secured but it remains to find the money necessary to pursue the work. In the great war, and indeed at all times, appeals made by the British Red Cross Society and the Order of St. John received the most generous response, showing that the heart of the Empire is with those who are risking their lives in support of the rights and liberties, not only of the peoples of the British Commonwealth of Nations, but of the whole civilised world.

We earnestly ask you to help the Joint Committee in the great work that lies before them. A fund is being opened in the name of the joint bodies. Donations should be sent to The Hon. Sir William H. Goschen, K.B.E., hon. treasurer, Red Cross and St. John Fund, at Messrs. Coutts & Co., 1, Park Lane, London, W.1.

DIPTEROUS LARVÆ AND WOUND TREATMENT

SIR,—When troops wounded in battle have been lying out on the ground, unattended for some time, their wounds very commonly become infested with larvæ of certain kinds of flies. In the war of 1914–18 W. S. Baer [1] noticed specially that when the wounds had acquired about their maximum maggot population they did not exhibit dangerous after-effects. On the other hand, men whose wounds had received prompt early treatment often developed infection. It was found that the presence of these larvæ was especially beneficial in cases of osteomyelitis. It was discovered that the larvæ were eating the necrotic tissue which was supporting the main bacterial infection and, at the same time, these larvæ were inhibiting further bacterial growth. Stewart [2] claimed that the scavenging larvæ play an important part in clearing the necrotic tissue, but that calcium carbonate, which is constantly excreted by the larvæ, is also important in alkalising the medium (the wound), in which the bacteria live, and of increasing phagocytic activity. The larvæ used in the earlier treatment of osteomyelitis belonged chiefly to the species *Lucilia sericata* (Meigen), *L. cæsar* (L.) and *Phormia regina* (Meigen). Stewart [3] showed, however, that due precautions must be taken and a proper knowledge of the biology of these larvæ is essential. Some species will feed on both necrotic and normal tissue and are potentially dangerous to the latter.

Much study has been devoted to the technique of rearing dipterous larvæ under aseptic conditions, and also of retarding their normal development, until they were actually needed for implantation within wounds. Sterilisation of the eggs in a 5 per cent. solution of formaldehyde, mixed with a 1 per cent. solution of sodium hydroxide, for five minutes has been found satisfactory by Robinson [4]; he gives full details of this process, and that of the subsequent rearing of the larvæ. Livingston and Prince [5] were successful in eliminating the inconvenience and unpleasantness associated with the actual "maggot therapy" by using a sterile extract of the creatures themselves. Robinson [6] claimed that the blow-fly larvæ contain allantoin in their excretion and that the rapid healing of wounds as the result of "maggot therapy" is due in the main to this agent. He did not claim, however, that it could be entirely substituted for the application of the living larvæ. Robinson carried his investigations further and found that a watery solution of allantoin provides the necessary healing agent, without the presence of dipterous larvæ at all. In 1935 allantoin was a rare chemical in the laboratory but it soon became to be made synthetically. Robinson also pointed out that a part of the allantoin molecule can be split off by hydrolysis to form urea. Further work led to the discovery that a 2 per cent. watery solution of urea has the equal healing properties of allantoin or of the fly larvæ themselves. It has the further advantage of being much cheaper than allantoin. Not only osteomyelitis, but many other kinds of non-healing wounds, have been treated in the manner just described—including gas-gangrene, heat burns, X-ray burns, and varicose and diabetic ulcers. So far as I am aware Paramorow in 1934 [7] was the first to use dipterous larvæ in the treatment of gas-gangrene. He applied maggots of the house-fly, *Musca domestica*, since calliphora larvæ were prone to devour healthy as well as necrotic tissue. He states that he cured three cases of gas-gangrene when amputation appeared inevitable, and that the healing process began 48 hours after the treatment began.

In this brief summary I have stated the present position of the subject in so far as it is known to me. It is desirable, at the present early stage in the world calamity that we are facing, that the foregoing information should be made as widely known as possible. There is no doubt that further research into the technique of this method is urgently required. Also, I believe that it is correct to say that this method of wound treatment has been more widely explored in the U.S.A. than in England. The literature on the subject is already extensive and I have only mentioned a few of the chief writings here.

I am, Sir, yours faithfully,

A. D. IMMS, F.R.S.

Zoological Laboratory, Cambridge, Sept. 7, 1939.

1. *J. Bone J. Surg.* 1931, **13**, 438.
2. *Surg. Gynec. Obstet.* 1934, **58**, 155.
3. *Ann. trop. Med. Parasit.* 1934, **28**, 445.
4. *U.S. Dept. Agric. Bur. Entom. Ser. E.* 1933, p. 311.
5. *J. Amer. med. Ass.* 1932, **98**, 143.
6. *J. econ. Ent.* 1937, **30**, 41.
7. *Z. wiss. Insektenbiol*, 1934, **27**, 82.

NEUROSIS OR PSYCHOSIS?

SIR,—Far be it from me at the present time to embark upon, or to encourage, controversy on this endless theme. As, however, you referred to my writings and views in the leading article from which this correspondence arose, I may perhaps be allowed to make two brief statements on the matter.

The first is that if the suggestion that an anxiety neurosis and a melancholic depression have anything in common with each other in either ætiology, symptoms, course or treatment, is to be accepted or even to pass unchallenged, I for one should feel that our terminology and psychopathology were futile from beginning to end, and should withdraw in despair from any further attempt at argument or discussion. I fancy that I should do so in fairly good company. The second is that it is unfortunately possible that we may all before very long have ample opportunity to observe the greatness of the gulf that separates neurosis from psychosis. I pointed out several years ago that no better help to the differential diagnosis exists than an air-raid. No-one who has experienced an air-raid in the company of a number of both neurotics and psychotics is likely ever again to be in doubt as to whether the difference between the two is "quantitative" or "qualitative." I need not say that I share the universal hope that we shall be spared this acid test, and I trust that Dr. Symonds and Dr. Gillespie may be able to compose their differences without having to wait for it. Of course, any observant mental-hospital physician who has noted the reaction of the patients in his "convalescent" wards to a thunderstorm could say a good deal about the profound difference between neurosis and psychosis, but his evidence would, I fear, be regarded as tainted.

Is it so very difficult to admit that even a psychosis must have a beginning, and that it may very often be undiagnosable or misdiagnosed at first, even by an experienced man? I cannot think that anything is gained—and the reputation of our specialty is certainly damaged—by confidently labelling an early, doubtful or undiagnosable psychosis as a neurosis, and endeavouring to have it both ways by asserting that the one may turn into the other.

I am, Sir, yours faithfully,

HENRY YELLOWLEES.

Harley-street, W.1, Sept. 11.

"DORMANT" LEAD POISONING

SIR,—I hope it may be my mistake, but I seem to detect some hint of superbity in Dr. R. E. Lane's comments on the above subject. His experience of industrial lead poisoning is not in question; his knowledge of lead poisoning in war conditions has yet to emerge. If he will read my letter again he will see that I have not ascribed symptoms to lead "that had been absorbed many years previously." These cases to which I referred had been absorbing lead up to the time of their joining the army, perhaps two or three years before I saw them, sometimes less. This is not "many years." A considerable incidence of lead poisoning, diagnosed on clinical and hæmatological grounds, was apparent for the first time after joining up. I should be more strictly accurate if I said that a considerable incidence of *acute* symptoms was seen; many of the older patients had suffered from constipation and other symptoms, possibly due to lead, for long periods. I claim to have made a clinical and hæmatological observation and to have drawn from it a not unreasonable deduction as to one aspect of lead intoxication. My case records perished long ago so that I cannot give precise details.

When Dr. Lane has had a similar experience he will be in a better position to plead for "a more critical attitude" and to condemn "a seemingly plausible explanation" as if his middle name was Tarquin. I trust he will not mislike the comparison.

I am, Sir, yours faithfully,

GORDON WARD.

Sevenoaks, Kent, Sept. 9.

A WAR-TIME PHARMACOPŒIA?

SIR,—In the present circumstances it is imperative to study forthwith means of preserving supplies of certain substances which, although widely prescribed, have little or no therapeutic value. Syrups, used solely as flavouring agents, edible oils and fats as ointment bases, alcohol in many tinctures, are instances of valuable substances which could be replaced. Belladonna pulverata, digitalis pulverata, and ergota preparata could be given in tablet form instead of the corresponding tinctures and extracts. This would mean the saving of alcohol and in addition, owing to the reduction in bulk, storage and transport problems would be simplified. *Now* is the time to devise a war-emergency pharmacopœia for the whole country. A small committee of representatives of the medical and pharmaceutical professions would have little difficulty in compiling a national formulary. Such a pharmacopœia is an urgent necessity.

I am, Sir, yours faithfully,

H. DAVIS,
Chief Pharmacist.

University College Hospital, London, W.C.1, Sept. 7.

EXPOSURE OF THE FACIAL NERVE

SIR,—Mr. Morris's article on the surgical treatment of facial paralysis (*Lancet*, 1939, Sept. 2, p. 558) prompts me to record an easy method of approach to the facial-nerve trunk. This I devised some forty years ago. I used to chisel off the tip of the mastoid process, with the insertion of the sterno-mastoid. The muscle and mastoid are turned downwards, thus exposing the nerve as it emerges from the stylo-mastoid foramen. It can then be followed with ease in either direction. I used this exposure first in cases of catarrhal palsy, which I now generally treat with diathermy.

I am, Sir, yours faithfully,

W. KENT HUGHES.

Melbourne, July 12.

FOR TRACHEOTOMY CASES

SIR,—I feel that arrangements should be made for patients who have to wear tracheotomy tubes to be given some protection against gas. Evacuation or if this is impossible their admission to a gas-proofed hospital ward would seem the most convenient way of dealing with the problem.

I am, Sir, yours faithfully,

W. A. MILL.

Harley-street, W.1, Sept. 11.

UNIVERSITY OF CAMBRIDGE.—We understand from Dr. Russell Reynolds that he has not resigned his examinership for the diploma in medical radiology, as stated in the *Cambridge University Reporter* and in our issue of Sept. 2. Dr. Kesley is taking his place for the October examination only.

PARLIAMENTARY INTELLIGENCE

ON THE FLOOR OF THE HOUSE

By MEDICUS, M.P.

FROM the day on which the Emergency Powers (Defence) Bill was passed through all its stages, including of course the royal assent, on Aug. 24 until to-day Parliament, the machinery of the defence services, the civil services, the industrial and business life of the nation and every other aspect of our lives have gone through a series of rapid changes. It is not only that Great Britain, the Dominions, India and the Colonial Empire have gone to war, it is that we have gone to war in an organised and deliberate way more like the stage of growth in some living creature than the work of millions of brains and millions of hands. The nation has been equipping itself for the possible danger of war in an intensive campaign ever since last year—and our preparations before that were on a great scale, but during that period the mind of Parliament and the nation has also been changing and equipping itself as perhaps never before in history.

When the final day had all but come and Parliament met on Friday and Saturday Sept. 1 and 2 there was not only organic change visible, there was a passion for righteousness visible as a consuming fire. When at 7.44 p.m. on Saturday Sept. 2 the Prime Minister rose to make his speech on the situation between Germany and Poland members were tense with expectation, for we had been sitting discussing important bills—but discussing while waiting for the all-important announcement expected. And when the Prime Minister's statement came it revealed delaying tactics by the Germans, failure to reply to the British demand that hostilities between Poland and Germany should cease, and a proposal from Italy for an immediate conference of Great Britain, France, Poland, Germany and Italy. It also contained a statement that Great Britain would not agree to a conference while Poland continued to be invaded, and that Great Britain did not recognise the German pretence to have annexed Dantzig to the German Reich. But it did not contain a declaration breaking off relations with Germany, and the passion in the hearts of M.P.'s of all parties swept into a tumultuous expression of anger. When Mr. Greenwood, leader of the Opposition, rose he was greeted, from the Tory benches, from the mouths of ex-cabinet ministers, from the Labour benches and from the Liberal benches with a roar asking for a lead for Britain. "Speak for England" called out two former Tory cabinet ministers; "Give a lead" called other members. Words could barely be heard in the roar of many voices expressing many feelings, but all united in the passionate desire to show unmistakably and definitely where Great Britain stood.

In that flame of a passion for righteousness the new Britain was born. The trend of events in Europe over a year had been paralleled by changes in the structure of our country like those in some vast chrysalis. Iron and steel and concrete defence taking the place of the softer structures of peace; large, swift acting and complex nervous mechanisms of central and departmental control superseding the more leisurely ways of normal days; new organs of offence in the air, on the sea and on land growing in power monthly, weekly, almost daily. And above all a change in spirit. Hatred of war among all classes, full realisation of horrors of war among all classes, and yet a determination, deep founded, expressed sometimes with difficulty but practically everywhere: "We've got to have done with this Hitler business." Then Parliament met on Sunday. The actual words of the Prime Minister in the House of Commons on Sunday morning were to announce the fact that during the night an ultimatum had been sent to Germany demanding a reply by 11 a.m., that no reply had been received and that we were in consequence, when the statement was made, already at war. All members had known this before from the air-raid warning which wailed over London soon after 11 a.m. But the actual words gave a feeling of profound relief. The change from the old order to the new was made. Britain was at war—not against Germany, but against Hitlerism.

* * *

Since Sept. 1 the work of Parliament has gone on regularly and in the new way—acts being passed by the dozen, often going through all their stages in one session, in order to give Government the powers it needs. Opposition and Government, not unity in one government but unity in a new form of association in which Opposition members act as critical advisers to the Government. The rights of discussion and free speech maintained, the freedom of the democracy carefully safeguarded for the future, the right of parliamentary criticism emphasised.

Already there have been two interesting medical results of that. On the Personal Injuries (Emergency Provisions) Bill introduced by Sir Walter Womersley, the Minister of Pensions, constructive criticism elicited that the Government were paying especial attention to the cases of head injuries and the "shell shock" class of case. On the main conscription measure, as the result of criticism, the Minister of War gave a definite undertaking that he would not send youths under 20 overseas unless the emergency demanded it and unless he had previously (if possible) consulted the House and given it the opportunity of criticism. The objection to sending boys of 18–20 overseas was the medical one that they were not hard enough for this work and that it was a waste of man power, because a a misuse of man power, to do it.

The work of Parliament is to go on. The House of Commons will meet usually each week and it will keep all vital matters under review. But it is a House with a new spirit. There is no division in the feeling that the nation has entered on a righteous war against Hitlerism and that it must be pursued until the Nazi government and all it stands for is swept out of existence. And after the War? Already men and women are thinking in terms very different from those of 1914–18. There are no heroics about this war and no heroics in Parliament.

The future must be remade, and remade on a basis of realistic and objective observation. Medical science and the other sciences will play a greater part in the future than they have in the past. The problem of adequate nutrition, for example, must cease to be a problem for all classes of the population.

From now onwards the mind of Britain is directed to the war. The great machine of offence and defence created by Democracy moves on; it will go on relentlessly and irresistibly, but it is not motived by hatred of any people, it is inspired by the love of freedom.

MEDICAL NEWS

Drug Fluctuations

The price of crude iodine has advanced by 30 per cent.; this will affect quotations for tincture of iodine, potassium iodide, sodium iodide and all iodine preparations. The price of quicksilver has also been raised by some 30 per cent., which will justify a rise in the cost of calomel, corrosive sublimate and all preparations of mercury. The cost of bismuth metal is higher, and makers of bismuth carbonate and other bismuth compounds have advanced their quotations by about 10 per cent. There has been a substantial increase in the cost of quinine sulphate and other quinine salts; prices are based on the Dutch florin which, like the American dollar, has moved against sterling; up to the present the rise in the price of quinine sulphate is about 20 per cent. Caffeine and theobromine are dearer to a similar extent, the prices of both being based on Dutch currency. To a smaller degree the prices of methyl salicylate, phenazone, benzoic acid, sodium benzoate, methyl salicylate and menthol have also been advanced. Practically all drugs of vegetable origin are dearer to a varying extent; in due course the higher prices will be reflected in quotations for tinctures, extracts and other galenical preparations, and also alkaloids. In the case of vegetable drugs dealers who hold supplies are rationing their clients, where it is necessary or advisable to do so, with a view to conserving stocks until these can be replenished. The same applies to medicinal essential oils. It should be mentioned that an addition of about 5 per cent. may be made to the price of all drugs in order to cover the war risk insurance of stock which is now compulsory.

Surgical Instruments Wanted

The regional commissioner for Scotland announces that as a result of the large hospital extensions, heavy demands are being made on manufacturers of surgical instruments and appliances. It would be a public service if private institutions and nursing-homes, medical men and firms, possessing surplus stocks, large or small, of the following would communicate with the Secretary, Department of Health for Scotland, 121A, Princes Street, Edinburgh: Artery forceps and other commonly used surgical forceps; surgical clamps; towel clips; hooks; retractors; surgical knives; osteotomes; hypodermic syringes; bedpans; catgut; irrigator stands; sterilising packs of any type; fish-kettles; accurate lotion thermometers for use in X-ray departments; and any other of the more common surgical instruments and apparatus. The department of health for Scotland is prepared either to purchase or to take on loan any of the articles mentioned provided, of course, that they are considered suitable.

Norwegian Tuberculosis Conference

The Nordisk Tuberkulose-Laegeforening held a conference in Trondheim from June 23 to 25, at which Denmark, Finland, Norway and Sweden were represented by their leading specialists. The two main subjects discussed were the relationship between the primary infection and destructive pulmonary tuberculosis, and the indications for thoracoplastic operations. Speaking on tuberculin tests one delegate mentioned that he has found that by repeating tests frequently on the same subjects it is not very rare to find definitely positive reactions giving place to negative reactions. It was generally agreed that considerable, if not absolute, protection can be conferred against tuberculosis by inoculating tuberculin-negative reactors with B.C.G., and approval was expressed of the principle of vaccinating with B.C.G. those who after the age of 12 are still tuberculin-negative even if they are not living in tuberculous surroundings. One of the most important communications was made by Dr. Andersson of Gothenburg where a follow-up study of about 1000 children inoculated with B.C.G. between 1927 and 1937 showed that not one of them had developed tuberculosis. On the invitation of Swedish tuberculosis specialists, it is hoped to hold the next conference in Sweden in 1941.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty held on Sept. 4, with Dr. John Henderson, the president, in the chair, Dr. James Cuthbert (Kelso) was admitted to the fellowship.

Commissions in the R.A.M.C. and the A.D.C.

Doctors who wish to place their services with the Army should register their names with the Central Emergency Committee of the British Medical Association, and should not apply direct to the War Office. Qualified dental surgeons wishing to obtain commissions in the Army Dental Corps should communicate with the Central Dental War Committee, 13, Hill Street, London, W.1, or, if resident in Scotland, with the Scottish Central Dental War Committee, care of the Department of Health for Scotland, Edinburgh, 2.

Emergency Medical Service

In the House of Commons on Sept. 7 the Prime Minister said that over 200,000 hospital beds were now ready for air-raid casualties; 56,500 of these were in the London region, 15,500 being inside the county and 41,000 outside. The beds in any region would of course be available to meet the needs of any other hard-pressed area. Over 11,000 trained nurses, 4000 assistant nurses and 50,000 auxiliary nurses had joined the Civil Nursing Reserve for service in hospitals or first-aid posts but more trained nurses and auxiliaries were needed, especially women who could give whole-time service in any part of the country. Nearly 2500 doctors had accepted enrolment in the emergency medical service and acceptances were being received daily.

Relief for Evacuated Persons

The Unemployment Assistance Board has been empowered to pay allowances to people in distress arising out of the war, even though they are not within the ordinary unemployment assistance scheme. Persons applying for relief must be over 16 and must prove evacuation from home under a Government plan and to be in need as a result; or that he or she, or the person on whom normally dependent for support, has been deprived entirely or to a substantial extent of normal means of livelihood by the war. Allowances will be calculated on the same scale as the ordinary unemployment assistance allowances and will be subject to generally similar provisions regarding the treatment of resources.

Hospitals in Northern Ireland

A general survey of the hospitals in Northern Ireland has been made and information has been collected of the number of existing beds, the number of additional beds which could be accommodated in existing premises, and as to the sanitary arrangements and equipment. The Minister of Home Affairs has appointed Dr. F. M. B. Allen to be Hospital Officer, and he has drawn up a memorandum in which the organisation of the Emergency Hospital Service is explained.

The hospitals have been classified into four groups. Group 1 includes the hospitals in Belfast which will receive general and special casualties, group 2 the hospitals outside Belfast which lie in areas in which casualties may also be expected to occur, and which will be expected to receive such casualties and also casualties from the outlying parts of Belfast.

The hospitals in group 3 are those situated outside the area in which casualties may be expected to occur and these will receive only unexpected casualties from their own neighbourhood, but will be expected to maintain medical services for ordinary patients who might otherwise go to hospitals in groups 1 or 2, and to receive such patients and convalescent casualties from hospitals in groups 1 and 2.

Group 4 is made up of hospitals in Belfast with specially limited equipment or accommodation upon which no demand will be made except in exceptional need.

EMERGENCY NOTICES

The examining board in England of the Royal Colleges of Physicians and Surgeons announces that: (1) The final L.R.C.P. and M.R.C.S. examinations, advertised to begin on Sept. 27, will, it is anticipated, begin on that date. Certain relaxations in the regulations for admission have been made. (2) The first examination in anatomy, physiology, materia medica and pharmacology, advertised to begin on Sept. 20, will, it is expected, begin on or about Oct. 18, and the date of entry has been extended to Tuesday, Sept. 26. In view of certain relaxations which have been made in the regulations for admission to this examination, candidates who have not already entered are advised to write at once to the secretary of the examining board. (3) The pre-medical examination in chemistry, physics and biology, advertised to begin on Sept. 18, will, it is expected, begin on or about Oct. 23, and the date of entry for the examination has been extended to Monday, Oct. 2. (4) Certain modifications in the conduct of these examinations are necessary, and candidates must be prepared to be examined outside London. (5) The offices of the secretary of the Examining Board in England, at the Examination Hall, Queen Square, London, W.C.1, will be open from 9 A.M. to 4 P.M. daily from Monday to Friday, and will be closed on Saturdays.

The temporary address of the central administrative offices of the University of London is Royal Holloway College, Englefield Green, Surrey.

The university session at Manchester will probably begin as arranged on Oct. 5. Students from St. Mary's Hospital medical school, London, will be transferred to Manchester to continue their studies there.

Full Term will probably begin at Oxford as arranged on Oct. 15.

University College, London, has moved to Aberystwyth, and communications should be sent to it there, care of University College of Wales.

The work of the Glasgow Post-Graduate Medical Association has been suspended indefinitely.

The central offices of the Queen's Institute of District Nursing are being moved to the Hermitage, East Grinstead. (Tel. East Grinstead 129.)

The offices of the *British Dental Journal* have been temporarily removed to 5, Westleigh Road, Barton Seagrave, Kettering. All the other activities of the British Dental Association will for the present be carried on at 13, Hill Street, W.1.

The Royal Sanitary Institute has cancelled its classes of instruction and sessional meetings until further notice. The work of the institute will continue to be carried out at 90, Buckingham Palace Road, Westminster, London, S.W.1, and should this become impossible at "Darroch," Harrow Road West, Dorking, Surrey. (Tel. Dorking 2877.)

The public and private business meetings of the Association of Industrial Medical Officers have been cancelled until further notice. Communications regarding the association should be addressed to the hon. secretary, Dr. D. Stewart, 50, Frederick Road, Edgbaston, Birmingham, 16.

The office of the Ross Institute of Tropical Hygiene has been moved to 29, Inglis Road, Ealing, London, W.5. (Tel. Acorn 1534.)

The annual meeting of the International Society of Medical Hydrology, announced to take place in Italy from Oct. 14 to 19, has been indefinitely postponed. The office of the society at 22, Bedford Place is being kept on for the present, but the October number of its *Archives of Medical Hydrology* will not be published, and general office activities are being reduced to a minimum.

The annual meeting of the British branch of the International League against Epilepsy has been abandoned.

It has been arranged by the sector office that the Central London Throat, Nose and Ear Hospital in Gray's Inn Road shall continue its normal work, as the other throat, nose and ear hospitals are closed.

The National Hospital for Diseases of the Heart, Westmoreland Street, W.1, has been closed, but has reopened for the reception of inpatients at Maids Moreton Hall, Buckingham. Doctors requiring information should apply to the R.M.O. at that address. (Tel. Buckingham 2235.)

The St. Thomas's Hospital old students' dinner, arranged for Oct. 6 at the Dorchester Hotel, has been cancelled.

Until further notice the address of the Medical Women's Federation will be 73, Bourne Way, Hayes, Bromley, Kent (Tel.: Hurstway 1904).

The London offices of the Royal Medical Benevolent Fund have been closed and the more important registers and records have been moved to Wormingford Grove, Wormingford, Essex. For the present it is impossible to consider giving financial help to any new applicants.

The emergency headquarters of the Pharmaceutical Society are at Birdgrove House, Mayfield, near Ashbourne, Derbyshire. The offices at 17, Bloomsbury Square, London, W.C.1, will remain open for the present to deal with urgent business. For the time being the *Pharmaceutical Journal* will be published at 23, Bloomsbury Square. The college of the society is housed at University College, Cardiff, and the various courses of instruction will be distributed between the University College of South Wales, the Technical College and the Welsh National School of Medicine. The society's pharmacological laboratories have been transferred to Reading. The September examinations have been postponed because a number of candidates have been called up for service.

The Royal Cancer Hospital, Fulham Road, are now able to receive and treat a limited number of cases of malignant disease. The outpatient and X-ray therapy departments are working as usual.

Royal Appointments

Sir Thomas Dunhill has been promoted sergeant-surgeon to the King and Colonel Benjamin Biggar, F.R.C.S., has been appointed hon. surgeon to the King in succession to Colonel J. M. Weddell, who has retired. Major-General Francis Casement, M.B., has been appointed hon. surgeon to the King in succession to Major-General H. M. J. Perry, who retires on Sept. 26. Mr. G. Gordon Bruce, F.R.C.S., is to be a surgeon to His Majesty in Scotland.

Arrangements at Ventnor

Realising that the war has thrown all efforts to treat tuberculosis into confusion, that many cases of tuberculosis have been discharged from sanatoria half-way through their treatment, that many others will be denied the benefits of treatment, and in addition that there will be many cases left in unsuitable, ill-ventilated, sandbagged houses who will be a danger to others, Dr. Fairley, the county medical officer of the Isle of Wight, has arranged with the Ministry of Health to take over two holiday camps to be run in conjunction with the Royal National Hospital for Consumption, Ventnor. It will accordingly be possible to deal with cases requiring treatment in bed in the hospital and with all ambulant cases in the holiday camps. It is hoped that ultimately there will be approximately 750 beds available. The camps will have a capacity of about 250 men and 100 women accommodated in 2- or 3-bed chalets. They will be reserved for *ambulant* cases of pulmonary tuberculosis, and patients will be expected to make their own beds, keep their chalets tidy, and generally assist in the work as far as their health allows. There will be a resident matron in each camp and any patient suffering from a relapse or any condition requiring treatment in bed will be transferred to the hospital.

WAR PREPARATIONS IN IRELAND

OUR Dublin correspondent writes: Although Ireland is not—for the present at any rate—a belligerent country, neither the authorities nor the public are neglecting the possibility of its becoming so, and preparations for emergencies arising out of the war are being rapidly pushed forward. The hospitals, as well as private householders, have been urged to render their buildings as secure as may be against the dangers of air-raids. It hardly needs emphasising that in the event of a raid reaching Dublin—whether by accident or design—the danger of fire from incendiary bombs would be very great, and there is no building in which a fire is so hard to combat as a hospital. It is, therefore, incumbent on the authorities of the hospitals to render the buildings as safe as may be, and it will probably be necessary in the first instance to arrange for the vacating of all top-storeys.

The provision of hospital accommodation for possible casualties has also to be studied. The Irish sweepstakes have not yet succeeded in adding appreciably to the number of general hospital beds in Dublin or Cork, and there is a definite shortage of hospital beds at present. To find accommodation in an emergency for some hundreds of additional hospital cases would be, in these present conditions, beyond the power of the Dublin hospitals, but it is understood that the question is being carefully considered.

The St. John Ambulance Brigade in Ireland, to which the country owes much both in peace and war in the past, has been very active both in training its personnel in air-raid precautions and in increasing the number of its members. For the past twelve months classes in first-aid and in A.R.P. have been held regularly, and have been attended by several hundreds of men and women. On Sept. 6, a public meeting to attract recruits for a special reserve of the brigade was held at the premises of the Royal Dublin Society, and the attendance was such as to surprise and even to embarrass the organisers. Over 2000 persons attended, and over 1400 fresh volunteers signed forms of application for various classes of voluntary service.

The Irish Red Cross Society—powers for the establishment of which was given by legislation last spring—has come into being. The Government nominated the first council, but in future the society is to be both self-supporting and self-managed. The President of Ireland (Dr. Douglas Hyde) accepted appointment as president of the society, and he nominated as chairman of the executive committee Mr. Charles MacAuley, F.R.C.S. The council is thoroughly representative and contains many members who have a long experience of work in societies with similar general service. Among these members are the commissioner of the St. John Ambulance Brigade in Ireland (Sir John Lumsden) and members of his district staff. Cordial coöperation between the brigade and the society is certain to be secured.

Appointments

BACON, EDWARD, M.B. Lond., D.O.M.S., hon. assistant ophthalmic surgeon to the Free Eye Hospital, Southampton.

DICK, ANDREW, M.D. Glasg., D.P.H., assistant county medical officer of health for Devon and district medical officer of health for the borough of Clifton-Dartmouth Hardness and urban districts of Brixham and Paignton.

HUGHES, JOHN, B.Chir. Camb., F.R.C.S., resident surgical officer at the Montagu Hospital, Mexborough.

JONES, IDRIS G., M.D. Lond., M.R.C.P., hon. assistant physician to the Cardiff Royal Infirmary.

JONES, T. B., M.R.C.S., D.P.M., medical superintendent at Bridge Home, Witham (branch of the Royal Eastern Counties Institution).

MACKAY, J. D., M.B. Aberd., D.P.H., temporary assistant medical officer of health for Barrow-in-Furness.

MACKINNON, N. A. M., M.B. Edin., D.P.H., deputy medical officer of health for Bury.

MELDRUM, C. B., M.B. St. And., junior assistant medical officer at the Argyll and Bute District Mental Hospital, Lochgilphead.

MILLS, W. G. Q., M.B. Camb., F.R.C.S., resident surgical officer at the Radcliffe Infirmary, Oxford.

NELIGAN, G. E., B.M. Oxfd., F.R.C.S., surgeon to the London Hospital.

NOWELL, STANLEY, M.B. Manc., D.M.R.E., junior assistant medical officer in the radiological department of the Manchester Royal Infirmary.

PEARSON, R. C. M., M.D. Edin., M.R.C.P.E., D.P.H., deputy medical officer of health for Middlesbrough.

PORTNOY, BENJAMIN, M.D. Manc., assistant medical officer in the massage and electrical department of the Manchester Royal Infirmary.

REID, D. A., M.B. Edin., F.R.C.S.E., resident surgical officer at Cumberland Infirmary, Carlisle.

SUTHERLAND, MARIE S., M.B. Aberd., D.P.H., deputy medical officer of health and deputy school medical officer for Accrington.

WILSON, G. F., L.M.S.S.A., temporary medical officer for casualty services for Epping and Ongar.

WOLFINDEN, C. R., M.D. Lond., D.P.H., assistant medical officer of health for Rotherham.

Births, Marriages and Deaths

BIRTHS

DOWLER.—On Sept. 8, wife of Dr. H. G. Dowler, of Churchdown, Gloucester—a daughter.

HATTON.—On Sept. 5, the wife of Dr. P. L. S. Hatton—a daughter.

JAMESON.—On Aug. 29, at Blackheath, the wife of Captain James Jameson, R.A.M.C.—a daughter.

O'MEARA.—On Sept. 5, at Catterick Camp, Yorks, the wife of Major F. J. O'Meara, R.A.M.C.—a son.

PESKETT.—On Sept. 4, the wife of Dr. G. L. Peskett, of Newport, Isle of Wight—a son.

SNOWMAN.—On Sept. 11, the wife of Dr. L. V. Snowman, of Finchley Road, London, a daughter.

TURTLE.—On Sept. 7, at Bournemouth, the wife of Dr. Peter de Bec Turtle—a daughter.

MARRIAGES

BALLINGER—LLOYD.—On Sept. 10, at Evesham, Owen David Ballinger, B.M., to Mary Lloyd.

CORBIN—BUNTING.—On Sept. 4, at Worcester, John Ogilvie Corbin, M.B., to Elisabeth Mary Bunting, M.B.

CROOK—DYSON.—On Sept. 4, at Crookham Parish Church, Aldershot, Lieutenant Anthony Crook, M.R.C.S., R.A.M.C., to Roberta May Brabazon Dyson.

GREEN—UNTHANK.—On Sept. 2, at Wokingham, Theodor Anton Green, F.R.C.S., to Susan Melinda Unthank.

HARRISON—BOWEN.—On Sept. 3, John Ormerod Harrison, F.R.C.S., to Mary Bowen.

HEISCH—NOBLE.—On Sept. 9, at Eastbourne, Ronald Brodie Heisch, M.B., to Auriel Margaret Noble.

LEARY—MCKINLAY.—On Sept. 7, at St. Columba's, Pont Street, Lieut.-Colonel Thomas Garnet Stirling Leary, A.A.M.C., to Annie Eileen McKinlay.

LOWN—KARKLINNIS.—On Sept. 2, at Epsom, Dr. J. F. Lown to Miss E. Karklinnis.

MCINTYRE—SHEED.—On Sept. 9, at St. George's, Hanover Square, Ivan Gordon McIntyre, M.B., to Anne Lowson Sheed.

MCLACHLAN—CANNING.—On Sept. 7, at All Souls', Langham Place, Angus Elrick William McLachlan, M.B., to Helen M. Canning.

OLLERENSHAW—TIMPSON.—On Sept. 6, at Didsbury Parish Church, Captain Robert George Watson Ollerenshaw, B.M., R.A.M.C. (T.), to Kathleen Mary Timpson.

PATON—REID.—On Sept. 10, at Aldeburgh Parish Church, Henry Oldham Paton, M.B., to Margaret Elizabeth Reid.

PEPPER—MACKENZIE.—On Sept. 9, at Amberley, Frank Richard Pepper, B.M., to Patricia Mackenzie.

ROSS—RUNGE.—On Sept. 4, at St. Marylebone Parish Church, Dr. T. A. Ross to Mrs. N. C. Runge.

SHAW—MACCOLL.—On Sept. 6, at Beaconsfield Parish Church, Colin Carter Shaw, M.R.C.S., to Daphne Vera MacColl.

SLOAN—HENRY.—On Sept. 8, at Guildford, David Robert Sloan, M.B., to Aileen Jeanne Henry.

STEWART—DICKINSON.—On Sept. 4, at Sunbury-on-Thames, Richard Arthur Stewart, M.C., M.B., to Alice Mary Dickinson.

WARING—THOMPSON.—On Sept. 6, at Totland, John William Brodie Waring, M.R.C.S., to Margaret Thompson.

WILLIAMS—HORTON.—On Sept. 9, at St. Marylebone Parish Church, Leslie Charles Williams, M.C., to Kathleen Miriam Horton, M.R.C.S.

DEATHS

BENSLEY.—On Sept. 6, at 13, Kelfield Gardens, London, W.10, George Egbert Bensley, M.R.C.S., assistant medical officer, public health department, London County Council.

CROOK.—On Sept. 8, Hugh Walter Dover Crook, M.R.C.S., D.P.M., assistant medical officer, Knowle Mental Hospital, Fareham, aged 36.

GRANT.—On Sept. 6, at Hampstead, Leonard Grant, M.D. Edin., formerly of New Southgate, aged 79.

LAWSON.—On Sept. 7, at Lowestoft, Hugh Lawson, M.R.C.S., late of Chislehurst.

LISTER.—On Sept. 6, at Johannesburg, Sir Frederick Spencer Lister, M.R.C.S., LL.D. Capetown, director of the South African Institute for Medical Research, aged 63.

NOTES, COMMENTS AND ABSTRACTS

THEY ALSO SERVE . . . . .

STANDING and waiting is at the moment the order of the day. What are all the doctors doing shut up in their hospitals ready for civilian casualties? Filling sand-bags, digging trenches, or darkening windows? At Guy's, at any rate, it was the students who were invited to turn the Park into a miniature western front (and some may interpret it as a sign of modern decadence, that the free beer supplied by the acting superintendent lasted longer than had been budgeted for).[1] At the Royal Free, it was the fair hands of the unqualified which heaped sand into bags. The doctors are at present, if not technically part of the great unemployed, at least part of the great unoccupied.

A few of us have the Napoleonic capacity for sleeping when, where, and for as long as, we like. For the rest, a few hints on passing the time pleasantly may not come amiss. Darts and billiards are apparently out of fashion, their places being taken by darts-bowls. Hospitals not blessed with tennis courts can still usually find a patch of grass where, before or after dinner, a delightful game may be played. A hospital without a shove-halfpenny board can hardly be called a hospital. Liquid refreshment should be stored in a cool place and, if supplies are limited, the key of the cave should be placed in trustworthy hands.

But, when all is said and done, there is no better way of passing time with pleasure and profit than with a pipe and book. Shall our emergency reading be light or heavy? Charity begins at home, so for a start, we would remind our readers that buried treasure may be found inside our own covers. We have known men who read Gibbon under shell-fire in the front line; with that mighty tale of revolutions, battles and sudden death as a background we see our own times in clearer perspective. Pepys, too, in the unbowdlerised version, is a sound piece of A.R.P. He lived, as we must now live, in day-tight compartments, extracting a maximum of pleasure from every trivial happening. Borrow selling his bibles in Spain transports us to another world. And each of these three books can stand constant interruptions and still survive.

For those who feel that in moments of relaxation a book should not strain the mind by either its matter or its method, there is always Dr. P. G. Wodehouse. His plots are intricate but they are of small importance. Sir Denison Ross recommends him to foreign students as a clue to the classics. Lord Dunsany makes one's imagination boggle in "The travel tales of Mr. Joseph Jorkeus." Bocaccio and O. Henry have the double merit of brevity and wit. Those who turn to Stephen Leacock may like to be reminded that he also wrote "How Lincoln freed the slaves." Light reading is not necessarily fiction. Professor Trevelyan's story of "The English revolution, 1688 to 1689" is not only easy, but also apt. Two hundred and fifty years ago, we got through the political growing-pains which now afflict another nation. But best of all is Fisher's "History of Europe," three volumes now happily printed on India paper as one. What a feast it is! We cross the Alps with Hannibal, the Rubicon with Cæsar, the Danube with Attila, and the Vistula with Napoleon, forgetting for a time the painful necessity of crossing the Saar with Gamelin. Fisher and a gas-mask will, we hope, see us through.

TOWN AND COUNTRY NITS

THE thoughtful countryman, confronted for the first time by a hoard of miniature townsmen, is asking himself if, along with other troubles, the evacuated children may not bring pediculi. A glance at the annual reports of the school medical officers suggests that this fear is groundless. In Devon, 98,657 inspections last year revealed 2244 "unclean" heads (2·3 per cent.). In East Sussex, pediculi were found in 1·9 per cent of inspected children, and in Warwickshire in 3·0 per cent. In urban areas, the figures are very similar. The borough of Bermondsey records only 0·8 per cent. discovered at 105,646 inspections. In the borough of Hendon 2·7 per cent. were found at 36,797 inspections. The city of Nottingham was high with 4·0 per cent. at 78,361 inspections. The complaint that the town child is dirtier than his country cousin is apparently no longer justifiable. Some say, however, that while the rural cleanliness may now be soundly based on parental pride the urban cleanliness still has the support of the de-lousing station. At the same time, in the general reshuffle, an occasional child with nits and pediculi may find its way into a home where these are unknown. This appears to have happened at Kettering, where a number of evacuees, chiefly unaccompanied children, were found, in the words of the *Northampton Evening Telegraph*, to be suffering from "certain skin diseases, not dangerous, but unpleasant." The borough council actually had to open a private house for treatment of the more obstinate cases. In Yorkshire, Alderman Davies, chairman of the North Riding public health committee, is urging medical examination of evacuees by evacuating authorities, now that the worst of the rush is over. Such a suggestion must be carefully considered before it is acted upon, for evacuation is more urgent than the detection of minor maladies. The Ministry proposes the removal from billets to empty houses of demonstrably unwelcome guests.

". . . The energies, the abilities, and the knowledge of each and every individual with scientific training must be directed without remission to the service of the Allied cause. Nevertheless, the end to be attained, and the end which science should hold ceaselessly before the eyes of the Allied peoples, is not destruction, but a constructive ideal—to ensure in the future such conditions as will make possible the advancement of all the peoples of the world without discrimination, according to the status and the traditions of each, in the light shed by reason and scientific knowledge. To keep alive the aims of science in furthering the pursuit of truth in the universe and the relation of that truth to the developments of man's nature, without regard to tribal and racial distinctions, should be, indeed must be, the ultimate function of the scientific thinker, whatever may be his more immediate preoccupations."—*Nature, Lond.*, Sept. 9, 1939, p. 455.

Medical Diary

TUESDAY, SEPT. 19.—4.30 P.M. (Tennent Memorial Building, 38 Church Street), Dr. I. Chesar Michaelson: Pressure Problems—Ocular, Cerebral and Circulatory.

Vacancies

Birmingham, Romsley Hill Sanatorium.—Res. Asst. M.O., at rate of £240.
Bolton Co. Borough, Townleys Hosp.—Third asst. M.O., £350. Also 4th asst. M.O., £250.
Burnley County Borough.—Sen. Asst. M.O.H., £800.
Chester Royal Infirmary.—2 Hon. Radiologists.
Dunedin Hosp., New Zealand.—Radiotherapist, £1100.
Hull Corporation Health Department.—Asst. M.O.H., £600.
Kettering and District General Hosp.—Jun. H.S. at rate of £150.
Metropolitan Hospital, Kingsland Road, E.8.—Resident Appointments at rate of £100.
Plymouth, Prince of Wales's Hosp., Greenbank Road.—H.S., at rate of £120.
Plymouth, Prince of Wales's Hosp.—Sen. and Jun. H.S.'s for Devonport section, at rate of £130 and £120 respectively.
Preston County Borough, Sharoe Green Hosp.—Jun. Asst. R.M.O. at rate of £100.
Reading, Royal Berkshire Hosp.—Res. H.S., H.P., and Cas. O., each at rate of £150.
Royal Chest Hospital, City Road, E.C.1.—H.P. at rate of £100.
St. Marylebone Borough Council.—Public vaccinators, £90 and £30 approx. (according to district).
Tottenham Borough.—Temporary Asst. M.O.H. (A.R.P.), £550.
Watford Borough.—Temporary Asst. M.O.H., £600.
Willesden General Hosp.—Cas. O., at rate of £100.

1. Passim, *Guy's Hosp. Gaz.* Sept. 9, 1939, p. 291.